

Señores

Superintendencia de Industria y Comercio

Dirección de Nuevas Creaciones

E. S. D.

Ref: Expediente No. NC2019/0005712.

**Solicitud de registro de Patente de Invención denominada
“COMPUESTOS BIFUNCIONALES PROTAC DIRIGIDOS A LA PROTEÍNA
TAU Y COMPOSICIONES FARMACÉUTICAS QUE LOS COMPRENDEN”.**

Fase nacional de la solicitud PCT/US2017/059604.

Solicitante: ARVINAS, INC.

Luz Helena Adarve, identificada como aparece al pie de mi firma, y obrando en mi condición de apoderada de **ARVINAS, INC.**, solicitante de la patente en referencia, a continuación, doy respuesta al Oficio **No. 5962** del 29 de abril de 2022.

1. Respecto a la fusión de solicitudes en trámite

En el numeral 1 del oficio No. **5962**, se presenta la siguiente recomendación sobre la fusión de solicitudes en trámite:

“Se encuentra coincidencia en la materia reclamada en las solicitudes NC2019/0005712, y las solicitudes NC2019/0007892, NC2019/0007091 (y su divisional NC2020/0010992) y NC2019/0007894, razón por la cual esta oficina recomienda fusionarlas en una única solicitud.

En el evento de no acoger la sugerencia, cada solicitud continuará con el trámite que le corresponde. Sin embargo, se le recuerda al solicitante que la misma materia no podrá tener doble patente”

Sobre esta sugerencia, el solicitante discrepa respetuosamente e indica que no desea fusionar las solicitudes en referencia. Adicionalmente sobre esto, también se

indica que las reivindicaciones se han modificado para especificar compuestos ULM-L-PTM, en donde los grupos ULM, L y PTM se seleccionan de fórmulas estructurales particulares que alejan a la presente solicitud de los objetos reclamados en las otras solicitudes.

2. Respecto a la patentabilidad de la solicitud

En el numeral 4 del oficio No. **5962**, se presentan las siguientes objeciones a la patentabilidad de las reivindicaciones de las reivindicaciones:

“Conforme a lo establecido en el literal d) del artículo 20 de la Decisión 486 de 2000 de la Comisión de la Comunidad Andina:

‘No serán patentables:

(...) d) los métodos terapéuticos o quirúrgicos para el tratamiento humano o animal, así como los métodos de diagnóstico aplicados a los seres humanos o a animales.’

Debido a lo anterior, esta oficina establece que el objeto de las reivindicaciones 34 a 39 no es patentable, toda vez que hacen referencia a métodos de tratamiento cuando reclaman: ‘para usar en un método con el propósito de tratar una enfermedad o trastorno relacionado con la proteína Tau en un sujeto, el método comprende administrar la composición a un sujeto que lo necesite, en donde el compuesto produce la degradación de la proteína Tau, de esta manera se trata o alivia al menos un síntoma de la enfermedad o trastorno’, lo cual no es patentable a la luz de la normatividad vigente”.

Para superar esta objeción, el solicitante presenta un nuevo capítulo reivindicatorio donde las reivindicaciones 34 a 39 fueron eliminadas.

3. Respecto al título de la solicitud

En el numeral 5.1 del oficio No. **5962**, se presentan las siguientes observaciones sobre el título de la solicitud:

“De conformidad con el literal d) del artículo 27 de la Decisión 486 de 2000 de la Comisión de la Comunidad Andina, el nombre de la invención de que se trata deberá reflejar el objeto y el campo industrial con el cual se relaciona la misma y ser concordante con la materia descrita y las reivindicaciones de la solicitud. El nombre no podrá referirse a nombres personales, marcas de productos o nombres de fantasía.

El título de la solicitud no refleja el objeto divulgado en la descripción y las reivindicaciones, por lo cual se sugiere el siguiente título: ‘COMPUESTOS BIFUNCIONALES PROTAC DIRIGIDOS A LA PROTEÍNA TAU Y COMPOSICIONES FARMACÉUTICAS QUE LOS COMPRENDEN’.

Con el objetivo de superar esta objeción, es deseo del solicitante enmendar el título de la solicitud de la siguiente manera:

“COMPUESTOS BIFUNCIONALES PROTAC DIRIGIDOS A LA PROTEÍNA TAU Y MÉTODOS ASOCIADOS DE USO COMPOSICIONES FARMACÉUTICAS QUE LOS COMPRENDEN”

De acuerdo con lo anterior el nombre de la invención debe quedar de la siguiente forma tal y como lo sugiere el examinador:

“COMPUESTOS BIFUNCIONALES PROTAC DIRIGIDOS A LA PROTEÍNA TAU Y COMPOSICIONES FARMACÉUTICAS QUE LOS COMPRENDEN”.

4. Respecto a las Objeciones a la Claridad y Concisión de las reivindicaciones (Artículo 30 de la Decisión 486).

En el numeral 5.2 del oficio No. **5962**, se presentan las siguientes objeciones a la claridad de las reivindicaciones:

- *“El pliego reivindicatorio no es conciso, cuando a lo largo de las reivindicaciones se observa la expresión: “sustituido” y “opcionalmente sustituido”, sin que posteriormente se encuentre la descripción de la sustitución pretendida y por tanto se sugiere realizar las delimitaciones en cada caso”.*

- *“Adicionalmente, el pliego reivindicatorio no es claro porque a lo largo del documento se observan páginas recortadas, estructuras incompletas y reivindicaciones que no permiten identificar la materia a proteger. Se sugiere realizar las correcciones adecuadas”.*
- *“Las reivindicaciones 1 y 2 presentan una excesiva complejidad y por tanto no son concisas, dado que a partir de ellas se podrían presentar múltiples opciones de distintos compuestos que exceden la materia sustentada en el capítulo descriptivo. Se sugiere delimitar adecuadamente la invención y adecuar la materia reclamada hacia los compuestos que tienen sustento en la descripción”.*
- *“La anterior objeción aplica para la reivindicación 16, la cual también es demasiado general. Se sugiere delimitar adecuadamente la invención”.*
- *“La reivindicación 1 no es concisa cuando reclama las siguientes definiciones: “[...] la ULM es una molécula pequeña de la porción de unión a la ligasa de ubiquitina E3 que une una ligasa de ubiquitina E3; la PTM es una porción de direccionamiento a la proteína Tau [...]”, con las cuales se pueden presentar múltiples opciones de distintas sustituciones que no tienen sustento en la descripción. Adicionalmente, la reivindicación 1 tampoco es clara ni concisa cuando menciona de manera general: “solvatos, polimorfos”, pero no realiza la correcta identificación de la (s) estructura (s) cristalina (s) a que se refiere. Se sugiere realizar las aclaraciones necesarias”.*
- *“La reivindicación 3 no es concisa cuando reclama los siguientes términos: “[...] alquilo, alquenilo, alquinilo, cicloalquilo, heterocicloalquilo, arilo o heteroarilo [...]”, con los cuales se pueden presentar múltiples opciones de distintas sustituciones que no tienen sustento en la descripción. Se sugiere mencionar el número de átomos y heteroátomos y el tipo de los mismos, en los casos que aplique heteroátomos”.*
- *“La anterior objeción aplica para las reivindicaciones 4 a 7, 9, 11 a 14, 17, 18, 20, 24 a 26 y 28, las cuales también emplean dichos términos ambiguos e imprecisos. Se sugiere delimitar adecuadamente la invención”.*
- *“La reivindicación 27 no es clara cuando menciona la expresión: ‘en donde el compuesto se selecciona del grupo que consiste en Compuestos 1-330*

(Tabla 1 y Tabla 2)”, con la cual se hace referencia a la descripción. Se sugiere mencionar los compuestos específicos de interés.

- “Las reivindicaciones 30 a 33 no son concisas cuando mencionan las expresiones: “[...] otro compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-29, o una de sus combinaciones [...]”, “[...]en donde el agente bioactivo adicional es un agente anti-neurodegenerativo [...]” y “[...]en donde el agente bioactivo adicional es un inhibidor de P-gp. [...]”, con las cuales se podrían presentar múltiples opciones de distintas composiciones que no tienen sustento en la descripción. Se sugiere definir correctamente cada componente de las composiciones reclamadas”.

Con el fin de superar las objeciones presentadas respecto a la claridad y concisión de las reivindicaciones, **es deseo del solicitante presentar un nuevo capítulo reivindicatorio compuesto por 14 reivindicaciones**, que encuentran su debido sustento en las reivindicaciones y la descripción originalmente presentadas, sin que ello conlleve ampliación de la invención.

Específicamente hacemos notar que las reivindicaciones se modifican con el fin de evitar una discusión extendida y así avanzar en el proceso de la solicitud de forma más rápida. La reivindicación 1 se modifica para incorporar las limitaciones de las reivindicaciones 8 (definición de PTM), 9 (definición de PTM), 14 (definición de VLM para respaldar la definición modificada de ULM), 17 (definición de CLM para respaldar la definición modificada de ULM) y 20 (definición de L). La reivindicación 1 se modifica adicionalmente para especificar C₁₋₆ para los grupos alquilo, haloalquilo, alquil-OH y alquilcarbonilo; C₃₋₁₁ para grupos cicloalquilo; C₆₋₁₀ para los grupos arilo; que los grupos heterociclilo tienen de 3 a 11 miembros y que los grupos heteroarilo tienen de 6 a 10 miembros. La reivindicación 15, correspondiente a la nueva reivindicación 3 enmendada, se modifica para eliminar las frases “grupos ... alquilo inferior y alcoxi”, “al menos una PTM, otra ULM (ULM’)” y “que acopla al menos una PTM o una ULM’ o ambas a la ULM-a”. La reivindicación 18, correspondiente a la nueva reivindicación 4 enmendada, se modifica para eliminar “N-alquilo” de la definición de W y modificar la definición de R_n para que comprenda “un grupo enlazador químico (L)”. La reivindicación 24, correspondiente a la nueva reivindicación 9 enmendada, se modifica para especificar que el alquilo C₁₋₆ lineal o ramificado y el alcoxi C₁₋₆ están opcionalmente sustituidos con 1-3 halógenos. La reivindicación 25, correspondiente a la nueva reivindicación 10 enmendada, se modifica para especificar arilo C₆₋₁₀, heteroarilo de 6-10 miembros, cicloalquilo de 3-11 miembros y heterocíclico de 3-10 miembros. La reivindicación 26,

correspondiente a la nueva reivindicación 11 enmendada, se modifica para eliminar la frase “o *fenilo*” y especificar el arilo de C₆₋₁₀. La reivindicación 27, correspondiente a la nueva reivindicación 12, se modifica para incluir los compuestos de las tablas 1 y 2 de la especificación. La reivindicación 28, correspondiente a la nueva reivindicación 13 enmendada, se modifica para especificar alquilo de C₁₋₆ o haloalquilo de C₁₋₆ en la definición de R¹⁰¹, R¹⁰², R¹⁰³, R¹⁰⁴, R¹⁰⁵, R¹⁰⁶, R¹⁰⁷, R¹⁰⁹, R¹¹⁰, R¹¹¹, R¹¹², R¹¹³, R¹¹⁴, R¹¹⁶, R¹¹⁷, R¹²⁰, R¹²¹, R¹²⁶, R¹²⁷, R¹²² y R¹²³. El soporte para todas las enmiendas a las reivindicaciones se puede encontrar, al menos, por ejemplo, en la página 18, párrafo [0066]; página 21, párrafo [0070]; página 22, párrafo [0071]; y los ejemplos 1 a 330 de la especificación tal como se presentó en fase internacional. Las reivindicaciones 10, 15, 18, 19 y 21 a 29, correspondientes respectivamente a las nuevas reivindicaciones 2 a 14 enmendadas, se modifican para actualizar sus dependencias y numeración. Las reivindicaciones 2 a 9, 11 a 14, 16, 17, 20 y 30 a 39 se eliminan.

A continuación, se explicará cómo este nuevo capítulo reivindicatorio busca superar cada una de las objeciones de claridad expuestas previamente:

- Sobre las objeciones a las expresiones “*sustituido*” y “*opcionalmente sustituido*”, que según el examinador se utilizan sin mostrar posteriormente la descripción de la sustitución prevista, el solicitante respetuosamente no está de acuerdo con esta aseveración. Sin embargo, únicamente con el propósito de agilizar el proceso de la solicitud, y de ninguna manera aceptando la validez de esta objeción, las presentes reclamaciones se modifican para eliminar los términos “sustituido” y “opcionalmente sustituido”.
- Sobre la objeción a la claridad del pliego reivindicatorio donde el examinador indica que no es claro porque a lo largo del documento se observan páginas recortadas, estructuras incompletas y reivindicaciones que no permiten identificar la materia a proteger, se indica que el capítulo reivindicatorio que se presenta junto con esta respuesta tiene sus páginas y estructuras completas.
- Sobre la objeción donde se objetan las reivindicaciones 1, 2 y 16 por ser supuestamente excesivamente complejas, poco concisas y por ir más allá de la materia sustentada en la descripción, el solicitante respetuosamente no está de acuerdo con esta aseveración. Sin embargo, únicamente con el propósito de agilizar el proceso de esta solicitud, y de ninguna manera aceptando la validez de la objeción, la reivindicación 1 se modifica para

incorporar las limitaciones de las reivindicaciones 8 (para aumentar la definición de PTM), 9 (para aumentar la definición de PTM), 14 (para aumentar la definición de ULM con base en la definición de VLM), 17 (para aumentar la definición de ULM con base en la definición de CLM) y 20 (para aumentar la definición de L); y se cancelan las reivindicaciones 2 y 16. En consecuencia, las presentes reivindicaciones son menos complejas y más concisas de acuerdo con el análisis del examinador. Además, las enmiendas a las presentes reivindicaciones se apoyan plenamente en la descripción de la solicitud. Por lo tanto, se solicita respetuosamente la reconsideración y el retiro de esta objeción.

- Sobre la objeción donde se rechaza la reivindicación 1 porque supuestamente no es concisa en vista de las frases “[...] *la ULM es una molécula pequeña de la porción de unión a la ligasa de ubiquitina E3 que une una ligasa de ubiquitina E3; la PTM es una porción de direccionamiento a la proteína Tau [...]*”, el solicitante respetuosamente no está de acuerdo con esta objeción. Sin embargo, únicamente con el propósito de agilizar el proceso de esta solicitud, y de ninguna manera aceptando la validez de esta objeción, la reivindicación 1 se modifica para eliminar la frase objetada en referencia, lo que hace que la objeción ya no sea procedente. Por lo tanto, se solicita respetuosamente la reconsideración y el retiro de esta objeción.
- Sobre la objeción donde se rechazan las reivindicaciones 3 a 7, 9, 11 a 14, 17, 18, 20, 24 a 26 y 28 porque supuestamente no son concisas en vista de los términos “*alquilo*”, “*alquenilo*”, “*alquinilo*”, “*cicloalquilo*”, “*heterocicloalquilo*”, “*arilo*” y “*heteroarilo*” en donde se alega que, en vista de estos términos, pueden surgir múltiples opciones de diferentes sustituciones que no están respaldadas por la descripción, el solicitante respetuosamente no está de acuerdo con esta severación. Sin embargo, únicamente con el propósito de agilizar el proceso de esta solicitud, y de ninguna manera aceptando la validez de esta objeción, el capítulo reivindicatorio se modificó para especificar el número de carbonos en cada uno de los “*alquilo*”, “*alquenilo*”, “*alquinilo*”, “*cicloalquilo*”, “*heterocicloalquilo*”, “*arilo*” y “*heteroarilo*”. Además, se cancelan las reclamaciones 3 a 7, 9, 11 a 14, 17 y 20. Por lo tanto, se solicita respetuosamente la reconsideración y el retiro de esta objeción.
- Sobre la objeción donde el examinador indica que la reivindicación 27 no es clara cuando menciona la expresión: “*en donde el compuesto se selecciona*

del grupo que consiste en Compuestos 1-330 (Tabla 1 y Tabla 2)” debido a que hace referencia a la descripción, se indica que la antigua reivindicación 27, correspondiente a la nueva reivindicación 12 enmendada, se modificó para ahora incluir los compuestos específicos de las tablas 1 y 2.

- Sobre la objeción donde se objetan las reivindicaciones 30 a 33 porque supuestamente no son concisas en vista de las frases “[...] otro compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-29, o una de sus combinaciones [...]”, “[...]en donde el agente bioactivo adicional es un agente anti-neurodegenerativo [...]” y “[...]en donde el agente bioactivo adicional es un inhibidor de P-gp. [...]”, donde se alega que, en vista de estas frases, podrían surgir múltiples opciones de diferentes composiciones que no están respaldadas por la descripción, el solicitante respetuosamente no está de acuerdo con esta objeción. Únicamente con el propósito de agilizar el proceso de esta solicitud, y de ninguna manera aceptando la validez de la objeción, el capítulo reivindicatorio que ahora se presenta elimina las antiguas reivindicaciones 30 a 33. Por lo tanto, se solicita respetuosamente la reconsideración y el retiro de esta objeción.

5. Respetto a la Determinación del Estado de la Técnica y al Examen de Patentabilidad

En los numerales 6, 7 y 8 del oficio citado, ese Despacho concluye que las reivindicaciones de la presente solicitud de patente carecen de novedad y nivel inventivo frente a las enseñanzas de los documentos **WO2016149668** (D1), **WO2016146985** (D2), **US2015291562** (D3) y **WO2015173225** (D4).

Con el fin de superar las objeciones presentadas respecto a la novedad y nivel inventivo de las reivindicaciones, **es deseo del solicitante presentar un nuevo capítulo reivindicatorio compuesto por 14 reivindicaciones**, que encuentran su debido sustento en las reivindicaciones y la descripción originalmente presentadas, sin que ello conlleve ampliación de la invención.

Primero se indica que la reivindicación se modificó con el objetivo de que sea aún más clara su novedad y nivel inventivo donde la reivindicación 1 ahora incluye las limitaciones las reivindicaciones 8 (definición de PTM), 9 (definición de PTM), 14 (definición de VLM para soportar la definición modificada de ULM), 17 (definición de CLM para soportar la definición modificada de ULM) y 20 (definición de L). La

reivindicación 1 enmendada ahora especifica compuestos de la forma ULM-L-PTM, donde el grupo PTM comprende un núcleo de anillo fusionado 6-5-6 o un núcleo basado en quinolina. Por el contrario, los compuestos del documento D1 tienen grupos PTM que comprenden un núcleo de anillo fusionado 5-7-5, un núcleo basado en ciclobutoxibenceno o un núcleo basado en tioxoimidazolidinona benceno. Estos grupos son estructuralmente muy diferentes a los compuestos especificados por las presentes reivindicaciones. Por lo tanto, el documento D1 no describe los compuestos especificados por las presentes reivindicaciones. Como tales, las presentes reivindicaciones son novedosas con respecto a la referencia D1 citada. Por lo tanto, se solicita respetuosamente la reconsideración y el retiro de esta objeción a la novedad.

5.1. Novedad

Aunque el Examinador haya citado los documentos D1, D2 y D3, para objetar la novedad de la presente invención, es posible afirmar que éstos no enseñan las características esenciales de la invención, como se explica a continuación.

Por su parte, se rechazan las reivindicaciones 1 y 2 por supuesta falta de novedad en vista del documento D2. El solicitante respetuosamente no está de acuerdo con esta objeción. Como se indicó anteriormente, la reivindicación 1 especifica compuestos de la forma ULM-L-PTM, donde el grupo PTM comprende un núcleo de anillo fusionado 6-5-6 o un núcleo basado en quinolina. Por el contrario, los compuestos del documento D2 tienen grupos PTM que comprenden un núcleo de anillo fusionado 5-7-5, un núcleo de anillo fusionado 6-7-5 y un núcleo basado en tetrahydroquinolina con un grupo N-acetilo. Estos grupos son estructuralmente muy diferentes a los compuestos especificados por las reivindicaciones que ahora se presentan. Por lo tanto, el documento D2 no describe los compuestos especificados por las presentes reivindicaciones. Como tales, las presentes reivindicaciones son novedosas con respecto al documento D2. Por lo tanto, se solicita respetuosamente la reconsideración y el retiro de esta objeción.

Por su parte, también se rechazan las reivindicaciones 1 y 2 por supuesta falta de novedad en vista del documento D3. En el oficio se alega que el documento D1 enseña “*un resto de unión a ubiquitina ligasa de Von Hippel-Lindau (VHL) E3 (ULM)*” y que el documento D3 menciona que “*CLM es un resto de unión de ubiquitina ligasa cereblon E3*” y que ambos anticipan el tema reivindicado en la reivindicación 2.

El solicitante respetuosamente no está de acuerdo con esta aseveración. La reivindicación 1 especifica compuestos de la forma ULM-L-PTM, donde el grupo PTM comprende un núcleo de anillo fusionado 6-5-6 o un núcleo basado en quinolina. Por el contrario, los compuestos del documento D3 tienen grupos PTM que comprenden un núcleo de anillo fusionado 5-7-5, un núcleo basado en ciclobutoxibenceno, un núcleo basado en tioxoimidazolidinona benceno, un núcleo basado en pirimidina-N(H)-benceno, o un núcleo basado en tiazolidinediona. Estos grupos son estructuralmente muy diferentes a los compuestos especificados por las presentes reivindicaciones. Por lo tanto, la referencia citada D3 no describe los compuestos especificados por las presentes reivindicaciones. Como se explicó anteriormente, los compuestos descritos en el documento D1 tampoco anticipan las presentes reivindicaciones. Por lo tanto, tomadas solas o en una combinación, los documentos D1 o D2 no anticipan las presentes reivindicaciones. Por lo tanto, se solicita respetuosamente la reconsideración y el retiro de esta objeción.

5.2. Nivel inventivo

Las anteriores reivindicaciones 3 a 33 se objetan por presuntamente carecer de actividad inventiva sobre las referencias citadas D3 y D4, en donde el oficio en referencia alega que una persona del oficio medianamente versada en la materia podría haber combinado los compuestos de la página 26 del documento D4 citado con los compuestos descritos en documento D3 citado y llegar a las reivindicaciones de la presente solicitud.

El solicitante respetuosamente no está de acuerdo con esta objeción de nivel inventivo. Las reivindicaciones que ahora se presentan especifican compuestos de la forma ULM-L-PTM, donde el grupo PTM comprende un núcleo de anillo fusionado 6-5-6 o un núcleo basado en quinolina. Por el contrario, los compuestos descritos en el documento D4 no son compuestos bifuncionales. Dicho de forma alternativa, los compuestos del documento D4 no contienen el enlace -L-ULM. Por lo tanto, el documento D4 no enseña ni sugiere los compuestos especificados por las presentes reivindicaciones.

El documento D3 no subsana las deficiencias de la mencionada referencia D4. En contraste con las reivindicaciones actuales, el documento D3 enseña compuestos que tienen grupos PTM que comprenden un núcleo de anillo fusionado 5-7-5, un

núcleo basado en ciclobutoxibenceno, una tioxoimidazolidinona de núcleo a base de benceno, un núcleo a base de pirimidina-N(H)-benceno o un núcleo a base de tiazolidindiona. Estos grupos son estructuralmente muy diferentes a los compuestos especificados por las presentes reivindicaciones. Como tal, el documento D3 no enseña ni sugiere los compuestos especificados por las presentes reivindicaciones. De hecho, una persona del oficio medianamente versada en la materia con conocimientos ordinarios en la técnica estaría motivada por el documento D3 para buscar compuestos con grupos PTM descritos allí porque esta referencia enseña que se logró una degradación >50% en células tratadas con 1 μ M de los compuestos 11, 13-16, 18-19, 21 y 22.

Por lo tanto, tomados individualmente o en combinación, los documentos D3 y D4 no enseñan ni sugieren los compuestos especificados por las presentes reivindicaciones. Como tales, las presentes reivindicaciones poseen actividad inventiva sobre las referencias de los documentos D3 y D3 citados. Por lo tanto, se solicita respetuosamente la reconsideración y el retiro de la objeción de nivel inventivo.

Por todo lo anterior se concluye que las reivindicaciones independientes en cuestión poseen características que no se dan a conocer de manera obvia para una persona versada en la materia por los documentos D1, D2, D3 o D4, por ende la presente invención debe ser considerada como novedosa y con nivel inventivo sobre el estado de la técnica presentado por el Examinador.

6. Conclusión

Las modificaciones realizadas a las reivindicaciones de la presente solicitud de patente y las aclaraciones presentadas a lo largo del presente escrito permiten superar completamente las objeciones realizadas a la claridad de las reivindicaciones, por lo cual, la presente solicitud cumple a cabalidad las exigencias establecidas por el artículo 30 de la Decisión 486 según los requerimientos del Examinador.

De otra parte, los argumentos expuestos en el numeral 5 del presente escrito ponen de manifiesto de una manera clara y contundente que lo revelado en las nuevas reivindicaciones de la presente solicitud resulta completamente NOVEDOSO E INVENTIVO sobre las enseñanzas del estado del arte más cercano representado

por los documentos D1; D2, D3 y D4, toda vez que nada dentro de dichos documentos revela en forma directa o al menos llega a sugerir todas las características que ahora se reclaman en la solicitud. Por consiguiente, no se puede derivar la inexistencia de los requisitos de ley para la concesión del privilegio de patentabilidad.

En consecuencia, me permito solicitar a ese Despacho, proceder con la revisión de las modificaciones y de los argumentos aquí presentados, para conceder el privilegio de patente solicitado para la materia objeto de las 14 reivindicaciones ahora presentadas en el capítulo reivindicatorio modificado, y que de subsistir alguna duda o inquietud respecto a la patentabilidad de la presente invención, a pesar de las modificaciones y argumentos técnicos ahora presentados, sin apartarse del espíritu inventivo originalmente revelado en la solicitud internacional, se le brinde la oportunidad al solicitante de aclararla o de limitar aún más la invención, mediante la emisión de un segundo examen de fondo, teniendo en cuenta el nuevo capítulo reivindicatorio que se somete a revisión, antes de que se emita una decisión definitiva por parte de ese Despacho, de conformidad con lo dispuesto en 1.2.2.5.1 del artículo primero de la Resolución 54093 de 2012.

7. Anexos

Junto con este escrito se incluye el capítulo reivindicatorio modificado, en donde se han llevado a cabo las modificaciones mencionadas anteriormente.

8. Pagos

Junto con esta respuesta se paga la tasa correspondiente a la modificación del capítulo reivindicatorio.

Petición

Solicito al Despacho, y en el evento que el examinador considere que pese a las modificaciones presentadas aún existen objeciones, que proceda a emitir un segundo examen de fondo sobre el nuevo capítulo reivindicatorio presentado.

En este sentido requiero se me comunique a través del SIPI o cualquier otro medio la existencia de estas objeciones para, de esta manera, si procede, realizar el nuevo pago del examen de patentabilidad de la solicitud de la referencia.

Atentamente,



LUZ HELENA ADARVE GÓMEZ.

C.C 41.575.435 de Bogotá.

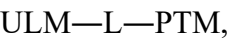
T.P. 14.884 C.S.J.

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REIVINDICACIONES (con marcas de modificación)

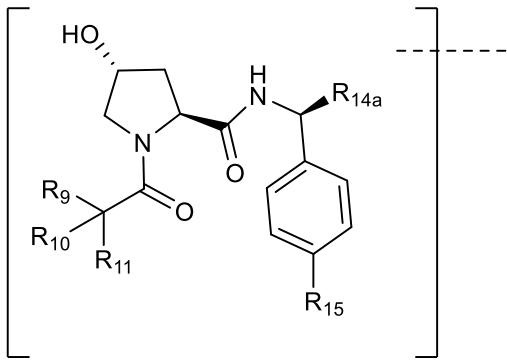
1. Un compuesto bifuncional que tiene la estructura química:



o una de sus sales, ~~enantiómeros, estereoisómeros, solvatos, polimorfos o profármacos~~
aceptables farmacéuticamente,

en donde:

la ULM está ~~una molécula pequeña de la porción de unión a la ligasa de ubiquitina E3 que une una ligasa de ubiquitina E3~~ representada por la estructura:

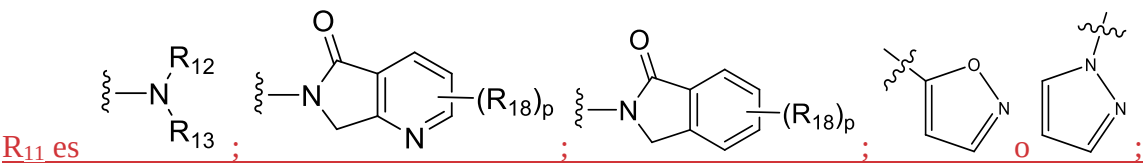


en donde:

es H, C₁₋₆ alquilo, C₁₋₆ haloalquilo, C₁₋₆ alquilo-OH, o ciclopropilo;

R₉ es H;

R₁₀ es H, etilo, isopropilo, tert-butilo, sec-butilo, ciclopropilo, ciclobutilo, ciclopentilo, o ciclohexilo;



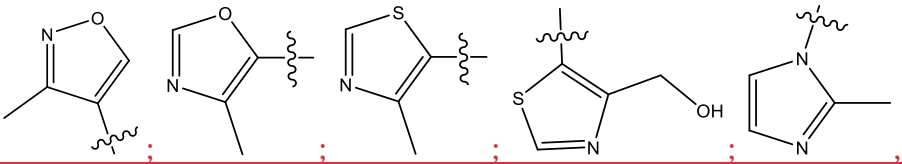
p es 0, 1, 2, 3, o 4;

cada R₁₈ es independientemente halo, alcoxi, ciano, alquilo, haloalquilo, haloalcoxi;

R₁₂ es H, C=O;

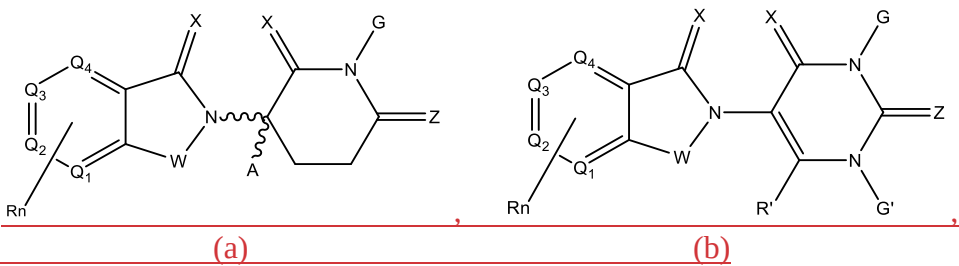
R₁₃ es H, C₁₋₆ alquilo, o C₁₋₆ alquilcarbonilo; y

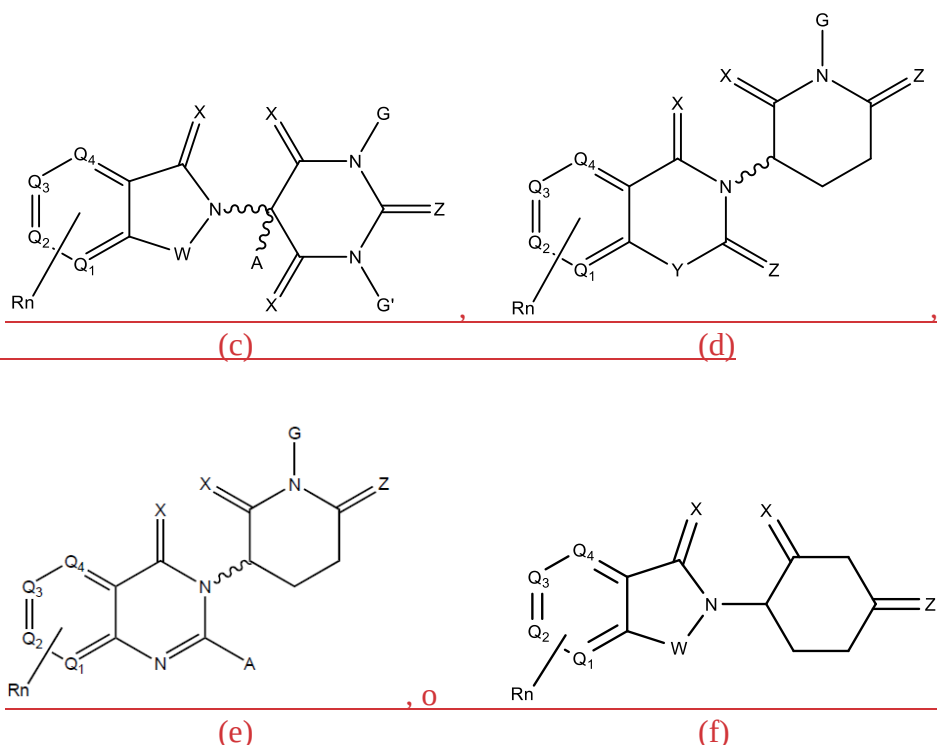
R₁₅ se selecciona del grupo que consiste en H, halógeno, CN, OH, y NO₂;



en donde la línea discontinua indica el punto de acoplamiento de una porción de enlazador químico;

o en donde la ULM está representada por la estructura:





en donde:

W se selecciona del grupo que consiste en CH₂, CHR, C=O, SO₂, y NH;

cada X se selecciona independientemente del grupo que consiste en O, S, y H₂;

Y se selecciona del grupo que consiste en CH₂, -C=CR', NH, O, y S;

Z se selecciona del grupo que consiste en O, S, y H₂;

G y G' se seleccionan independientemente del grupo que consiste en H, alquilo, OH, R'OCOOR, R'OCONRR'', y bencilo opcionalmente sustituido con R';

Q₁, Q₂, Q₃, y Q₄ representan un carbono C sustituido con un grupo independientemente seleccionado de R', N o N-óxido;

A se selecciona independientemente del grupo H, Cl y F;

R comprende -CONR'R'', -OR', -NR'R'', -SR', -SO₂R', -SO₂NR'R'', -CR'R'', -CR'NR'R'', -P(O)(OR')R'', -P(O)R'R'', -OP(O)(OR')R'', -OP(O)R'R'', -Cl, -F, -Br, -I, -CF₃, -CN, -NR'SO₂NR'R'', -NR'CONR'R'', -CONR'COR'', -NR'C(=N-CN)NR'R'', -C(=N-CN)NR'R'', -NR'C(=N-CN)R'', -NR'C(=C-NO₂)NR'R'', -SO₂NR'COR'', -NO₂, -CO₂R', -C(C=N-OR')R'', -CR'=CR'R'', -CCR', -S(C=O)(C=N-R')R'', -SF₅, o -OCF₃;

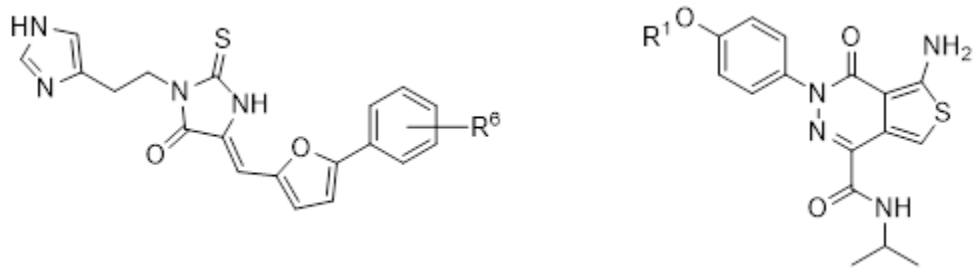
R' y R'' se seleccionan independientemente del grupo que consiste en un enlace, H, N, N-óxido, o -C(=O)R;

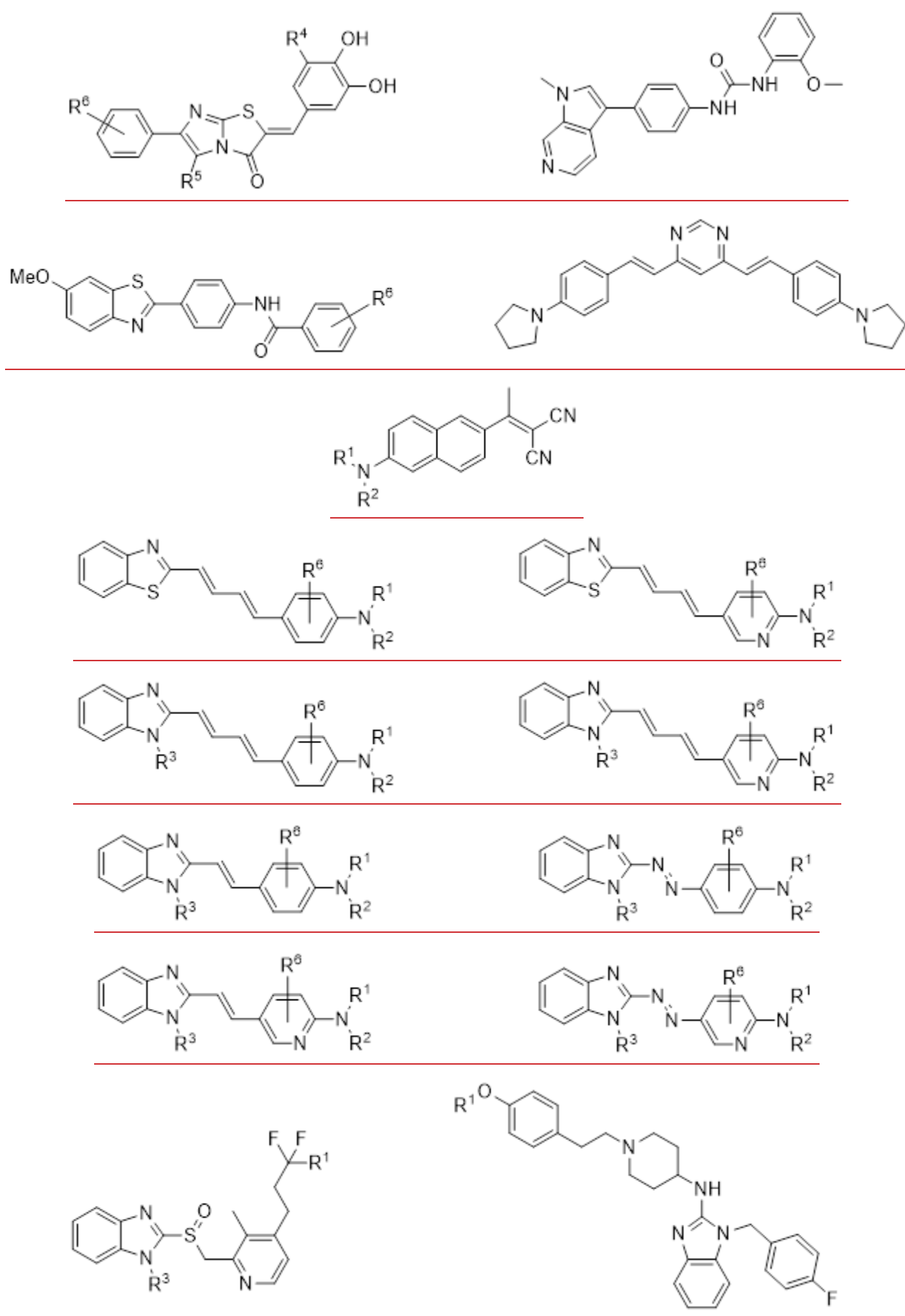
~~~~ representa un enlace que puede ser estereoespecífico ((R) o (S)) o no estereoespecífico;

y

en donde n es un número entero de 1-4;

la PTM está una porción de direccionamiento a la proteína Tau representada mediante una estructura química seleccionada del grupo que consiste en:





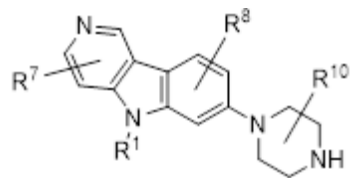
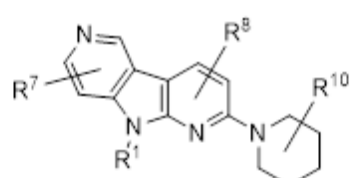
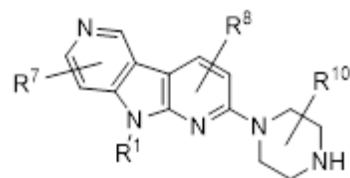
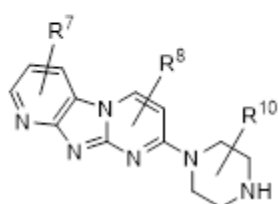
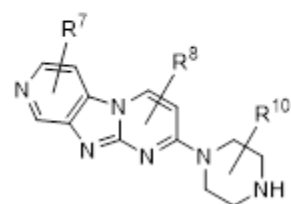
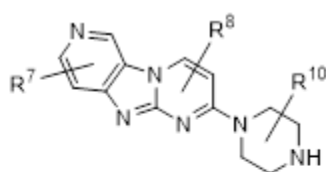
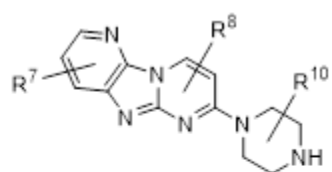
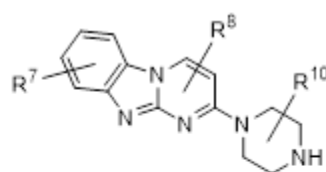
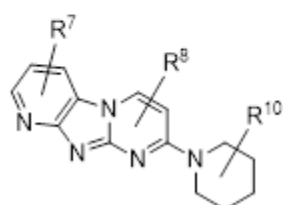
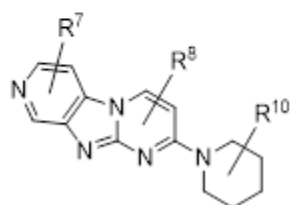
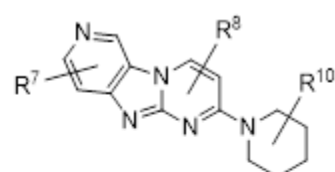
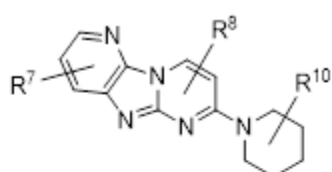
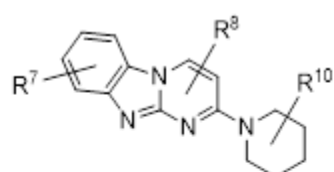
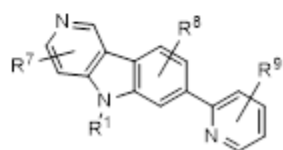
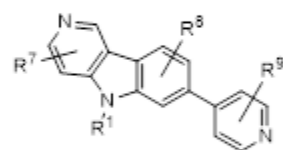
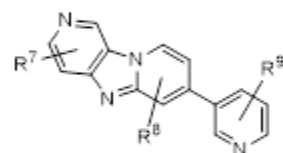
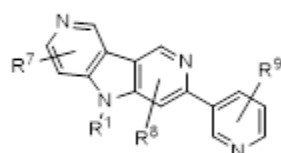
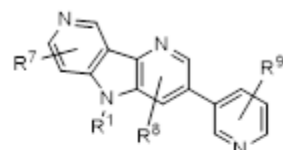
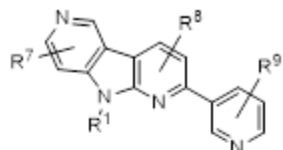
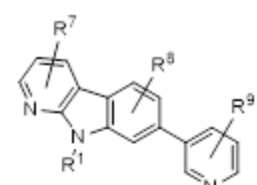
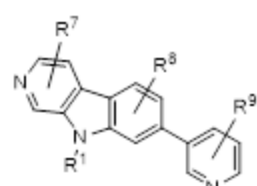
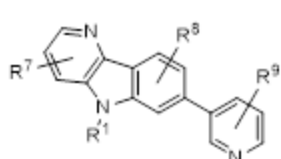
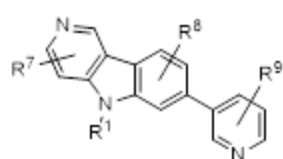
en donde:

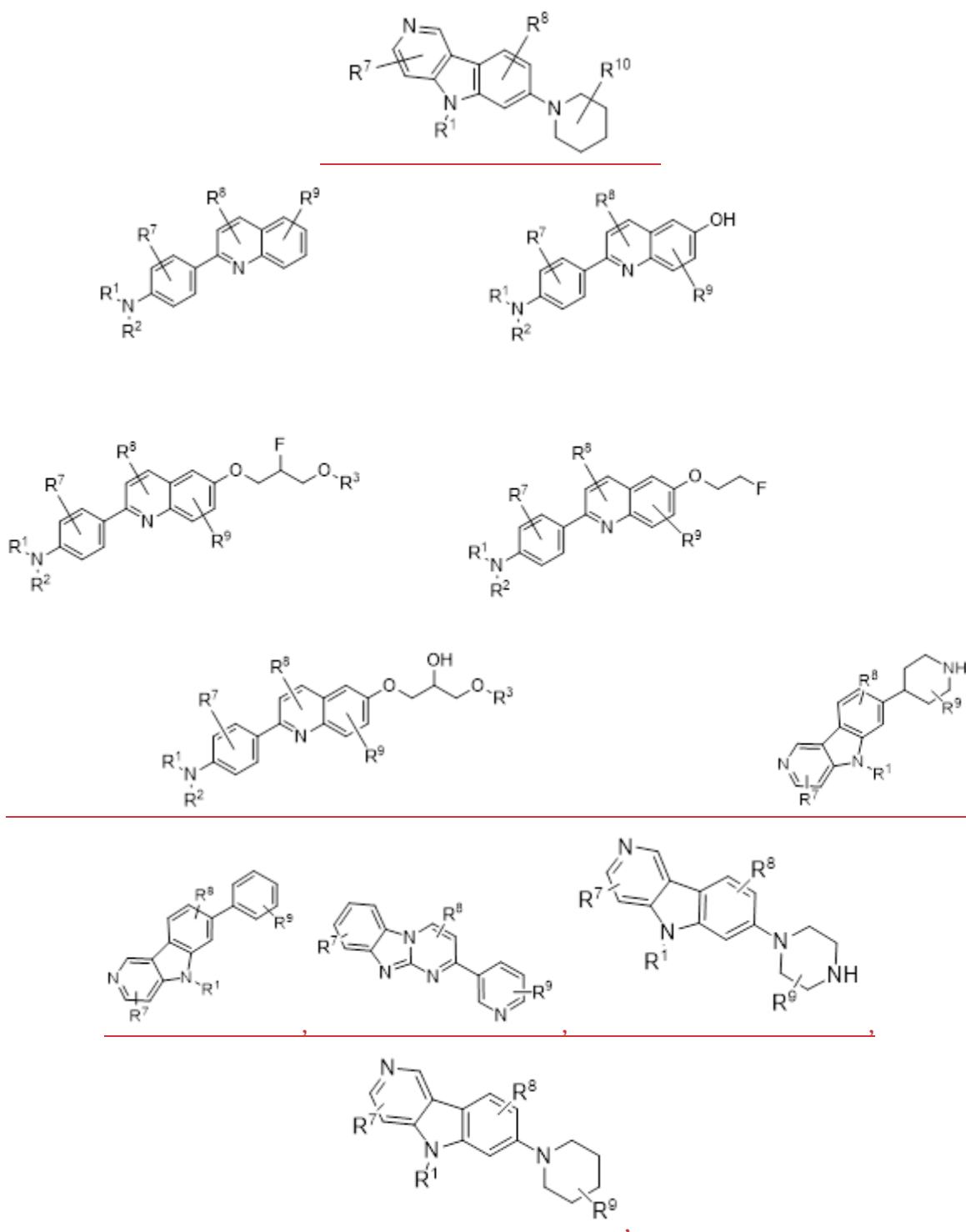
R<sup>1</sup>, R<sup>2</sup> y R<sup>3</sup> se seleccionan independientemente de H, metilo, etilo, 2-fluoroetilo y 2,2,2-trifluoroetilo;

R<sup>4</sup> y R<sup>5</sup> se seleccionan independientemente de H, metilo, etilo y halógeno; y

R<sup>6</sup> es 1 a 2 sustituyentes independientemente seleccionados de H, metilo, etilo y halógeno;

o la PTM se representa mediante una estructura química seleccionada del grupo que consiste en:





en donde:

$R^1$ ,  $R^2$  y  $R^3$  se seleccionan independientemente de H,  $C_{1-6}$  alquilo opcionalmente sustituido

1-3 veces con halo; y

$R^7$ ,  $R^8$ ,  $R^9$  y  $R^{10}$  son 1 a 8 sustituyentes independientemente seleccionados de H,  $C_{1-6}$  alquilo,

$C_{1-6}$  haloalquilo, halógeno, hidroxilo, amino, acetilamino, o ciano; y

el L está ~~un enlace o una porción de unión química que conecta ULM y PTM~~ representado por la fórmula:



en donde:

A es un grupo que se conecta a la porción ULM o PTM; y

q es un número entero mayor que o igual a 1,

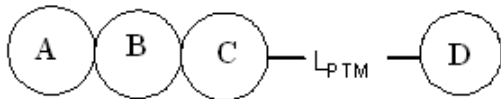
en donde A se selecciona del grupo que consiste en, un enlace,  $CR^{L1}R^{L2}$ , O, S, SO,  $SO_2$ ,  $NR^{L3}$ ,  $SO_2NR^{L3}$ ,  $SONR^{L3}$ ,  $CONR^{L3}$ ,  $NR^{L3}CONR^{L4}$ ,  $NR^{L3}SO_2NR^{L4}$ , CO,  $CR^{L1}=CR^{L2}$ ,  $C\equiv C$ ,  $SiR^{L1}R^{L2}$ ,  $P(O)R^{L1}$ ,  $P(O)OR^{L1}$ ,  $NR^{L3}C(=NCN)NR^{L4}$ ,  $NR^{L3}C(=NCN)$ ,  $NR^{L3}C(=CNO_2)NR^{L4}$ ,

cicloalquilo de C<sub>3-11</sub> opcionalmente sustituido con grupos 0-6 R<sup>L1</sup> y/o R<sup>L2</sup>, heterociclilo de 3-11 miembros opcionalmente sustituido con grupos 0-6 R<sup>L1</sup> y/o R<sup>L2</sup>, C<sub>6-10</sub> arilo opcionalmente sustituido con grupos 0-6 R<sup>L1</sup> y/o R<sup>L2</sup>, heteroarilo de 6-10 miembros opcionalmente sustituido con grupos 0-6 R<sup>L1</sup> y/o R<sup>L2</sup>, donde R<sup>L1</sup> o R<sup>L2</sup>, cada uno independientemente se unen opcionalmente a otros grupos para formar C<sub>3-11</sub> cicloalquilo y/o heterociclilo de 3-11 miembros, opcionalmente sustituidos con grupos 0-4 R<sup>L5</sup>;

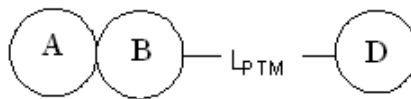
R<sup>L1</sup>, R<sup>L2</sup>, R<sup>L3</sup>, R<sup>L4</sup> y R<sup>L5</sup> son, cada uno independientemente, H, halo, alquilo de C<sub>1-8</sub>, OC<sub>1-8</sub>alquilo, SC<sub>1-8</sub>alquilo, NHC<sub>1-8</sub>alquilo, N(C<sub>1-8</sub>alquilo)<sub>2</sub>, C<sub>3-11</sub>cicloalquilo, heterociclilo de 3-11 miembros, OC<sub>1-8</sub>cicloalquilo, SC<sub>1-8</sub>cicloalquilo, NHC<sub>1-8</sub>cicloalquilo, N(C<sub>1-8</sub>cicloalquilo)<sub>2</sub>, N(C<sub>1-8</sub>cicloalquilo)(C<sub>1-8</sub>alquilo), OH, NH<sub>2</sub>, SH, SO<sub>2</sub>C<sub>1-8</sub>alquilo, P(O)(OC<sub>1-8</sub>alquilo)(C<sub>1-8</sub>alquilo), P(O)(OC<sub>1-8</sub>alquilo)<sub>2</sub>, CC-C<sub>1-8</sub>alquilo, CCH, CH=CH(C<sub>1-8</sub>alquilo), C(C<sub>1-8</sub>alquilo)=CH(C<sub>1-8</sub>alquilo), C(C<sub>1-8</sub>alquilo)=C(C<sub>1-8</sub>alquilo)<sub>2</sub>, Si(OH)<sub>3</sub>, Si(C<sub>1-8</sub>alquilo)<sub>3</sub>, Si(OH)(C<sub>1-8</sub>alquilo)<sub>2</sub>, COC<sub>1-8</sub>alquilo, CO<sub>2</sub>H, halógeno, CN, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, NO<sub>2</sub>, SF<sub>5</sub>, SO<sub>2</sub>NHC<sub>1-8</sub>alquilo, SO<sub>2</sub>N(C<sub>1-8</sub>alquilo)<sub>2</sub>, SONHC<sub>1-8</sub>alquilo, SON(C<sub>1-8</sub>alquilo)<sub>2</sub>, CONHC<sub>1-8</sub>alquilo, CON(C<sub>1-8</sub>alquilo)<sub>2</sub>, N(C<sub>1-8</sub>alquilo)CONH(C<sub>1-8</sub>alquilo), N(C<sub>1-8</sub>alquilo)CON(C<sub>1-8</sub>alquilo)<sub>2</sub>, NHCONH(C<sub>1-8</sub>alquilo), NHCON(C<sub>1-8</sub>alquilo)<sub>2</sub>, NHCONH<sub>2</sub>, N(C<sub>1-8</sub>alquilo)SO<sub>2</sub>NH(C<sub>1-8</sub>alquilo), N(C<sub>1-8</sub>alquilo) SO<sub>2</sub>N(C<sub>1-8</sub>alquilo)<sub>2</sub>, NH SO<sub>2</sub>NH(C<sub>1-8</sub>alquilo), NH SO<sub>2</sub>N(C<sub>1-8</sub>alquilo)<sub>2</sub>, NH SO<sub>2</sub>NH<sub>2</sub>.

2. ~~El compuesto de conformidad con la reivindicación 1, en donde la porción de unión a la ligasa de la ubiquitina E3 se dirige a una ligasa de ubiquitina E3 seleccionada del grupo que consiste en Von Hippel-Lindau (VLM) y cereblon (CLM).~~

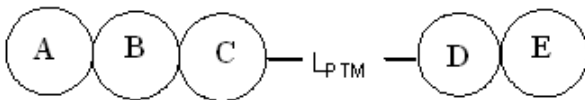
3. ~~El compuesto de conformidad con la reivindicación 1 o 2, en donde la PTM se representa mediante al menos uno de la Fórmula I-XI:~~



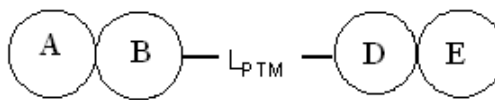
I



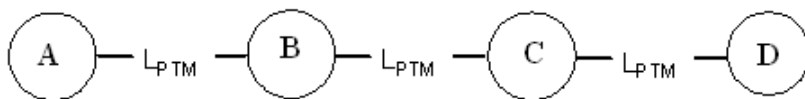
II



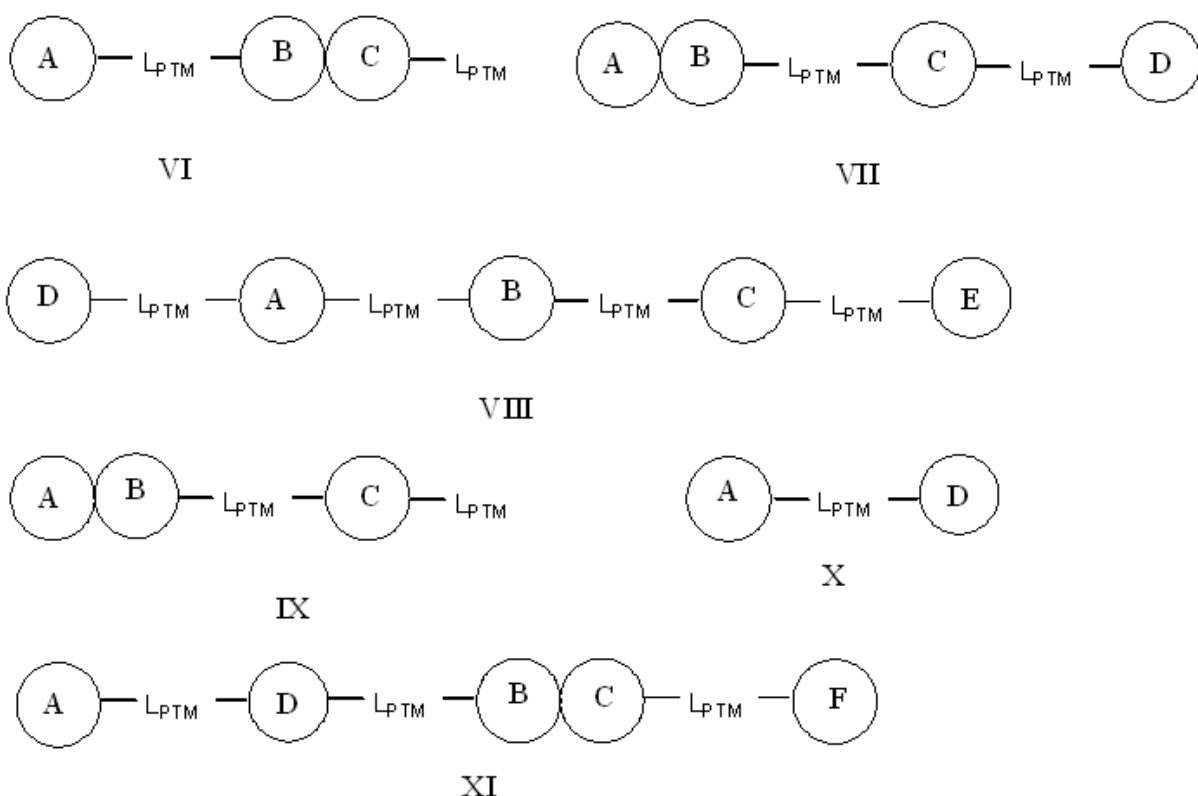
III



IV



V



en donde:

A, B, C, D, E, y F se seleccionan independientemente de un anillo arilo o heteroarilo de 5 o 6 miembros opcionalmente sustituidos, un cicloalquilo de 4 a 7 miembros opcionalmente sustituido o un heterocicloalquilo, donde el contacto entre los círculos indica la fusión de los anillos;

L<sub>PTM</sub> se selecciona de un enlace, un alquilo, un alquenilo o un alquinilo, opcionalmente interrumpidos por uno o más anillos (es decir, cicloalquilo, heterocicloalquilo, arilo o heteroarilo), o uno o más grupos funcionales seleccionados de los grupos —O—, —S—, —NR<sup>1</sup><sub>PTM</sub>—, —N=N—, —S(O)—, —SO<sub>2</sub>—, —C(O)—, —NHC(O)—, —C(O)NH—, —NH—SO<sub>2</sub>—, —NHC(O)NH—, —NHC(O)O—, o —OC(O)NH—, en donde el dicho grupo funcional se localiza opcionalmente en ambos extremos del enlazador; y

R<sup>1</sup><sub>PTM</sub> se selecciona de H o alquilo.

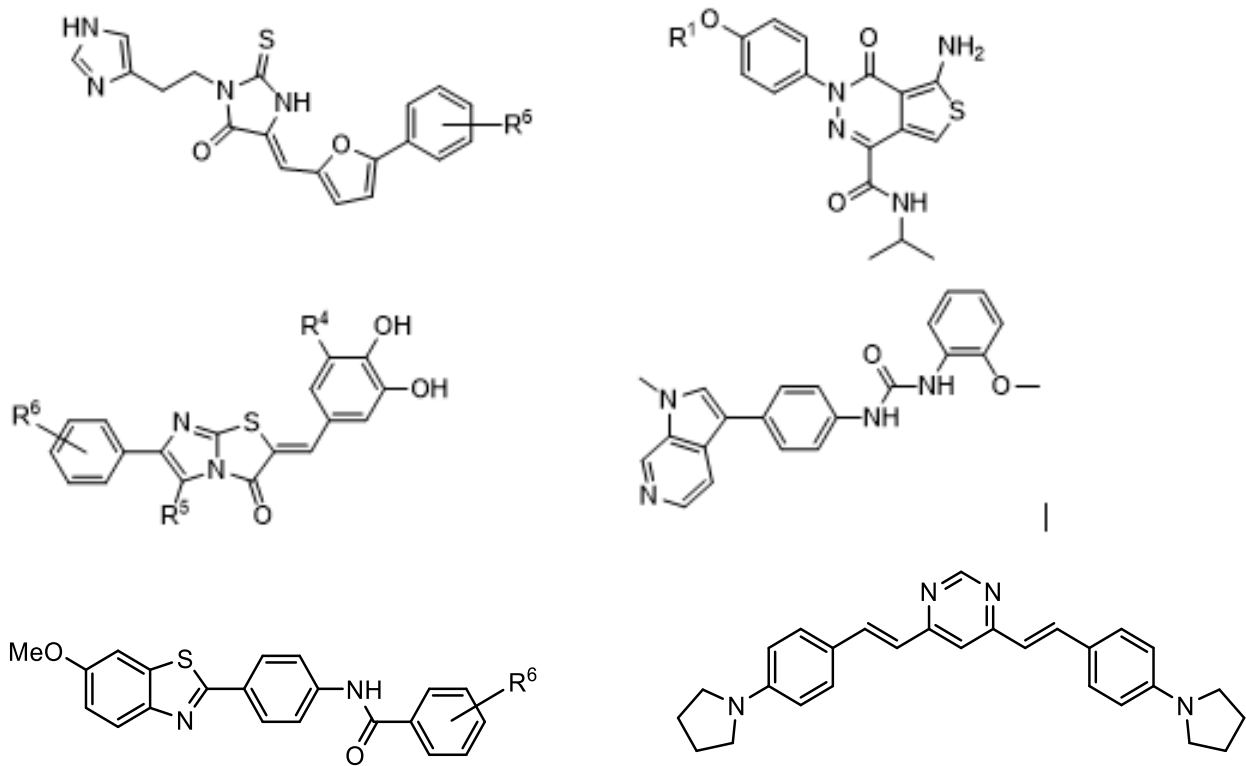
4. El compuesto de conformidad con la reivindicación 3, en donde al menos uno de:
  - al menos uno de A, B, C, F, o una de sus combinaciones se selecciona de anillos arilo o heteroarilo de 5 o 6 miembros opcionalmente sustituidos;
  - los anillos arilo y heteroarilo de A, B, C, D y E de PTM se sustituyen opcionalmente con 1–8 sustituyentes cada uno independientemente seleccionado de alquilo, alquenilo, haloalquilo, halógeno, hidroxilo, alcoxi, fluoroalcoxi, amino, alquilamino, dialquilamino, acilamino, trifluorometilo y ciano, en donde los dichos grupos alquilo y alquenilo además se sustituyen opcionalmente; o
  - una de sus combinaciones.
5. El compuesto de conformidad con la reivindicación 3, en donde la PTM es la Fórmula I y:
  - los anillos A, B y C son independientemente anillos arilo o heteroarilo fusionados de 5 o 6 miembros;

~~L<sub>PTM</sub> se selecciona de un enlace o un alquilo; y~~  
~~D se selecciona de un arilo, heteroarilo o heterocicloalquilo de 6 miembros,~~  
~~en donde A, B, C y D se sustituyen opcionalmente con alquilo, haloalquilo, halógeno,~~  
~~hidroxilo, alcoxi, amino, alquilamino, dialquilamino, trifluorometilo o ciano.~~

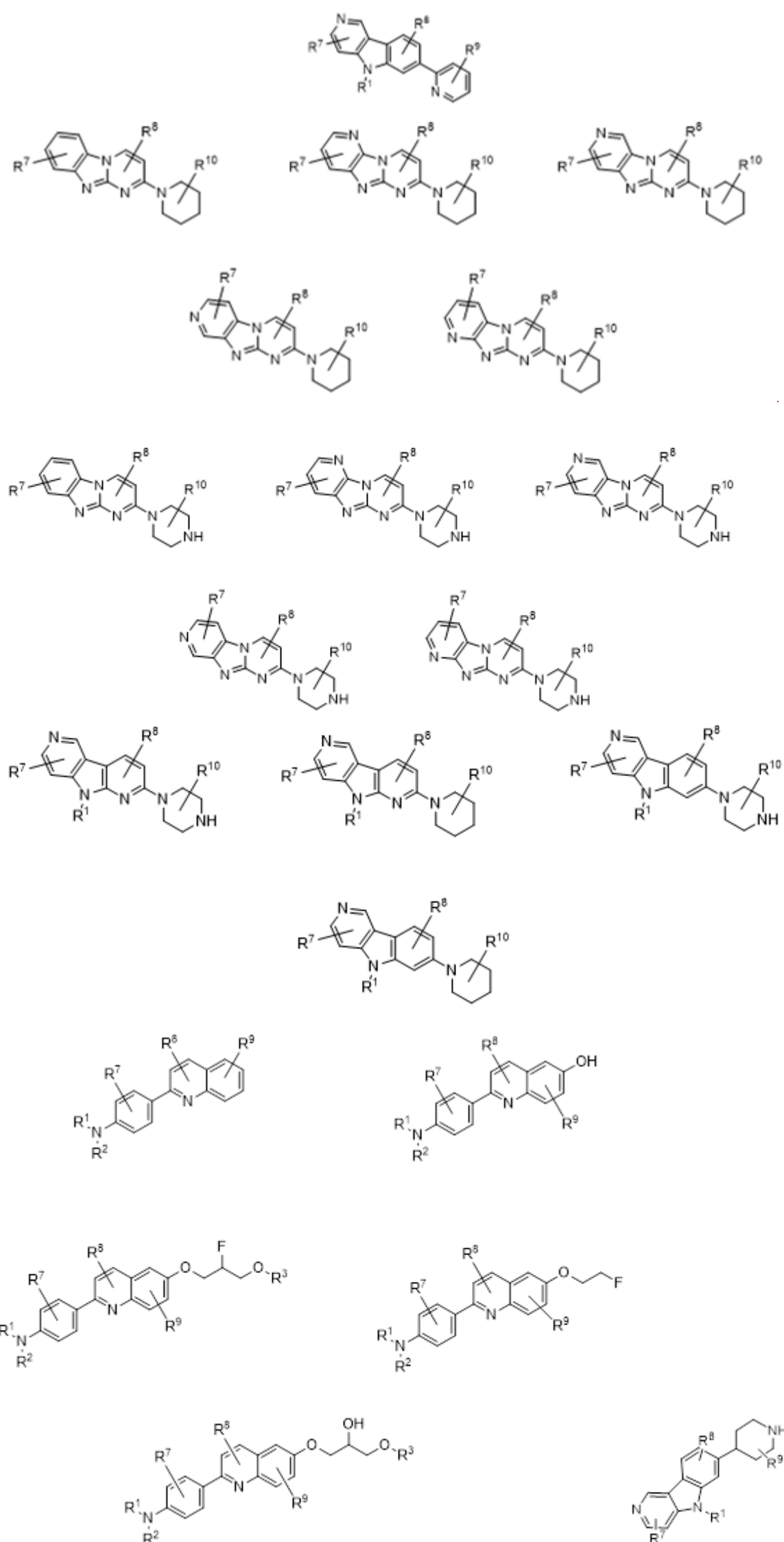
~~6. El compuesto de conformidad con la reivindicación 3; en donde la PTM es la Fórmula I y:~~  
~~A y C son un fenilo o un anillo heteroarilo de 6 miembros;~~  
~~B es un anillo heteroarilo de 5 miembros;~~  
~~L<sub>PTM</sub> es un enlace; y~~  
~~D es un anillo heteroarilo de 6 miembros o un heterocicloalquilo de 6 miembros,~~  
~~en donde cada uno de A, B, C y D se sustituye opcionalmente independientemente con~~  
~~alquilo, haloalquilo, halógeno, hidroxilo, alcoxi, amino, dialquilamino, trifluorometilo, o~~  
~~ciano, y en donde un átomo de nitrógeno de cualquiera de los anillos A, B, C y D no se~~  
~~conecta directamente a un heteroátomo o a un átomo de carbono, al que se une~~  
~~directamente otro heteroátomo.~~

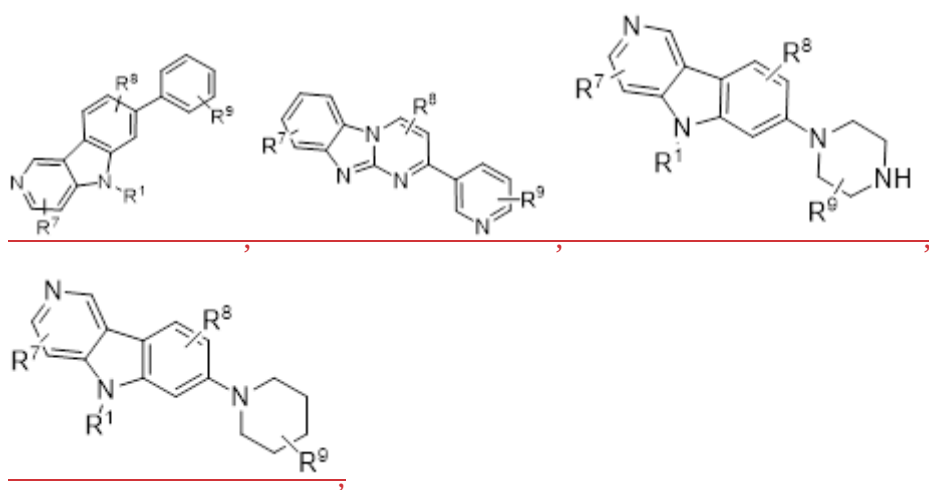
~~7. El compuesto de conformidad con la reivindicación 3; en donde la PTM es la Fórmula III o~~  
~~IV y:~~  
~~A, B y C son anillos arilo o heteroarilo fusionados de 5 o 6 miembros;~~  
~~L<sub>PTM</sub> se selecciona de un enlace o un alquilo; y~~  
~~D y E son anillos arilo o heteroarilo fusionados de 5 o 6 miembros;~~  
~~en donde A, B, C, D y E se sustituyen opcionalmente con alquilo, haloalquilo, halógeno,~~  
~~hidroxilo, alcoxi, amino, alquilamino, dialquilamino, trifluorometilo, o ciano.~~

~~8. El compuesto de conformidad con cualquiera de las reivindicaciones 1-3, en donde la~~  
~~PTM se representa mediante una estructura química seleccionada del grupo que consiste~~  
~~en:~~







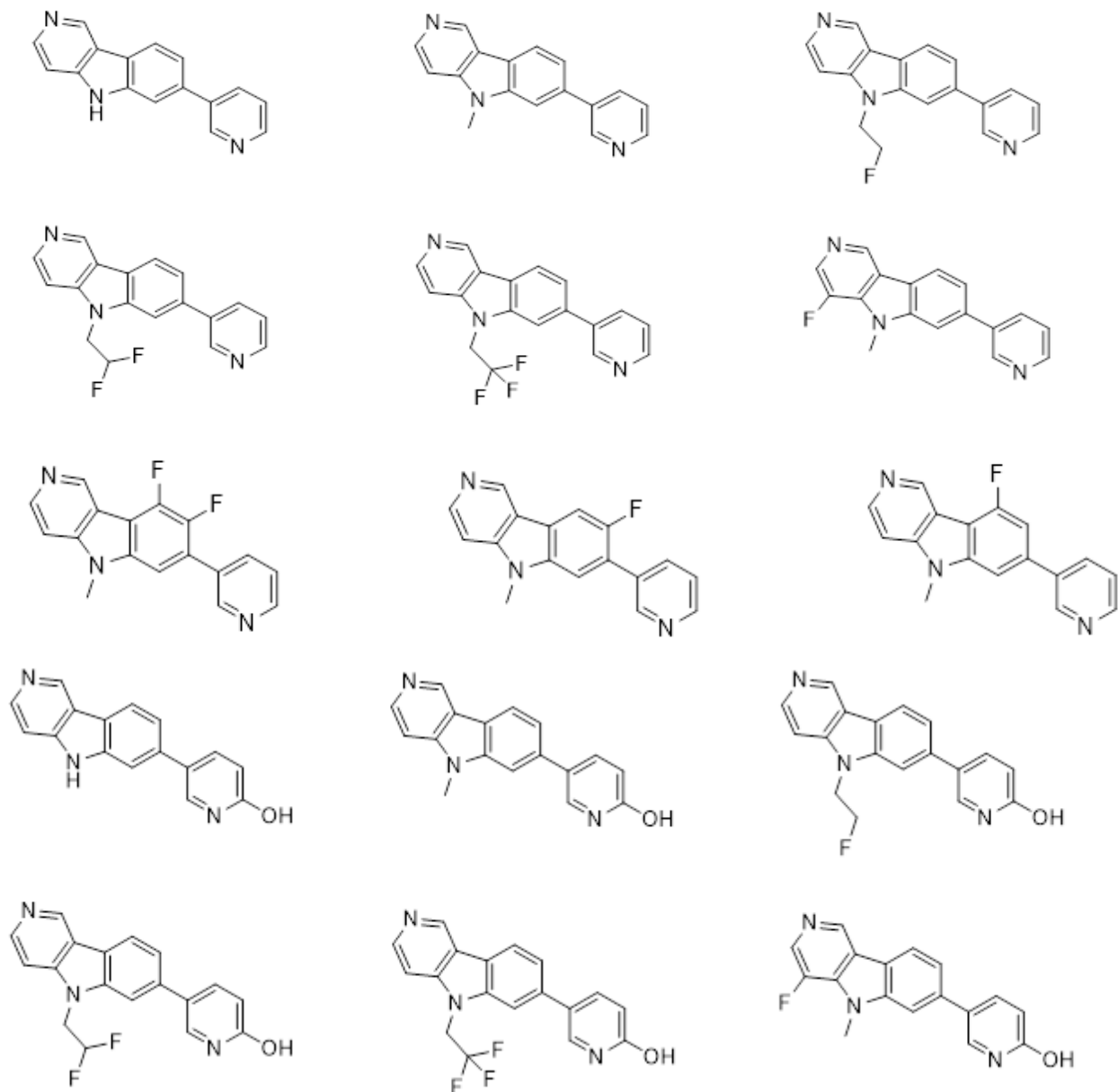


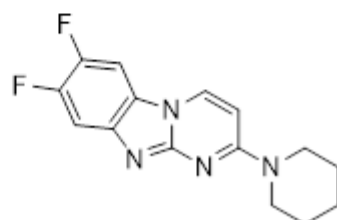
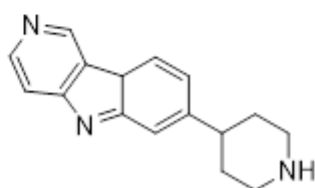
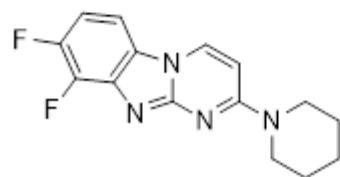
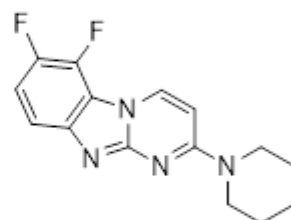
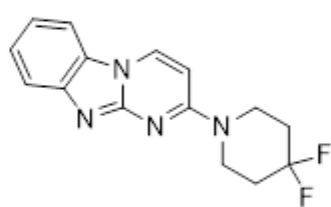
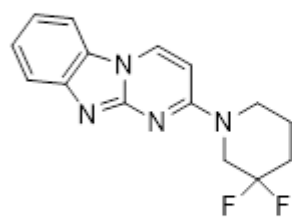
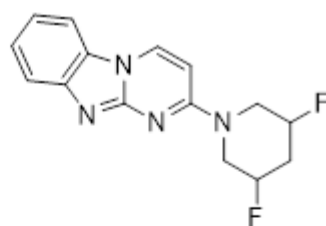
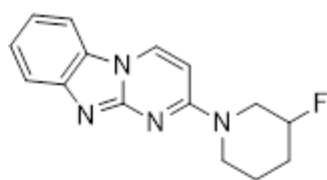
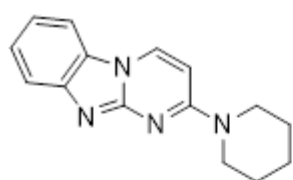
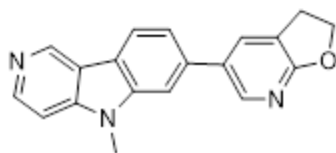
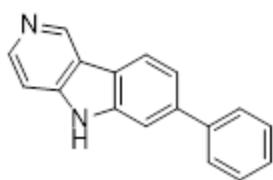
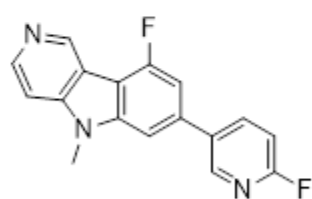
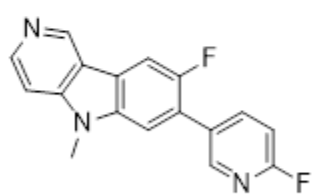
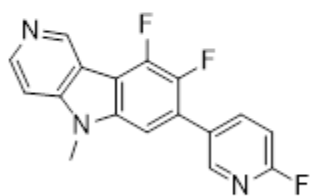
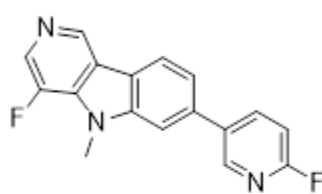
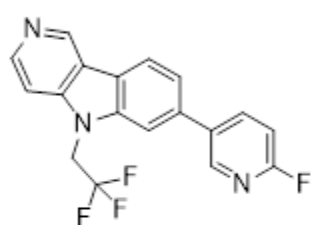
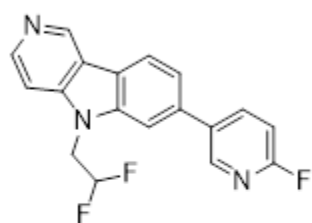
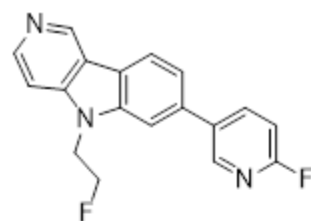
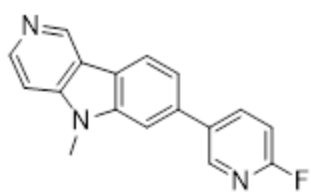
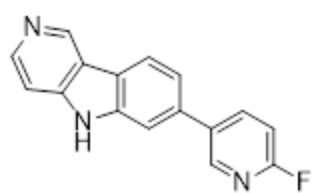
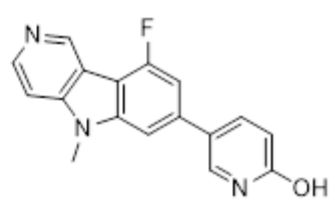
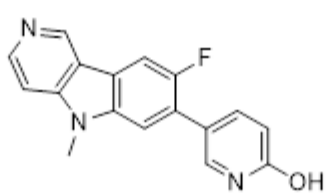
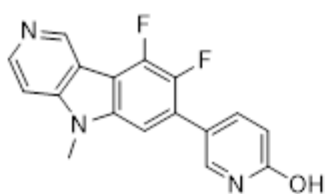
en donde:

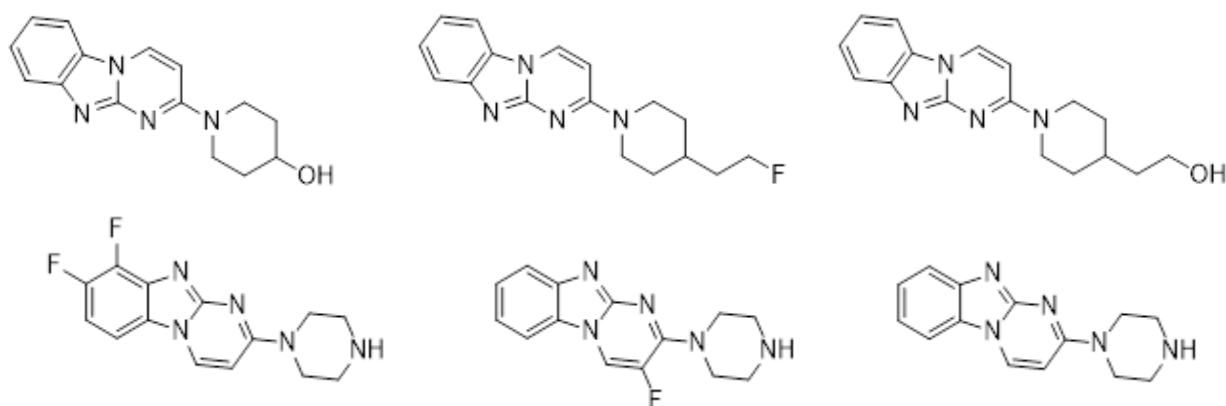
$R^1$ ,  $R^2$  y  $R^3$  se seleccionan independientemente de H, alquilo opcionalmente sustituido, metilo, etilo, 2-fluoroetilo y 2,2,2-trifluoroetilo; y

$R^7$ ,  $R^8$ ,  $R^9$  y  $R^{10}$  son 1 a 8 sustituyentes independientemente seleccionados de H, alquilo opcionalmente sustituido, haloalquilo, halógeno, hidroxilo, alcoxi, amino, dialquilamino, acetilamino, trifluorometilo, o ciano.

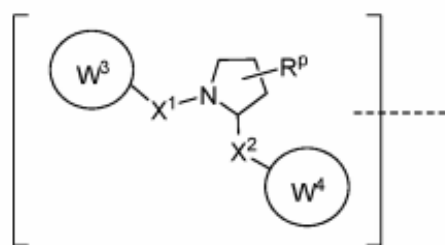
102. El compuesto de conformidad con ~~cualquiera de las reivindicacion~~reivindicaciones 1-3 o 9, en donde la PTM se representa mediante una estructura química seleccionada del grupo que consiste en:







11.—El compuesto de conformidad con cualquiera de las reivindicaciones 1-10, en donde la ULM es una porción de unión a la ligasa (VLM) Von Hippel-Lindau (VHL) representada por la estructura:



en donde:

$X^1, X^2$  se seleccionan cada uno independientemente del grupo que consiste en un enlace, O,  $NR^{Y3}$ ,  $CR^{Y3}R^{Y4}$ , C=O, C=S, SO, y  $SO_2$ ;

$R^{Y3}, R^{Y4}$  se seleccionan cada uno independientemente del grupo que consiste en H,  $C_{1-6}$  alquilo lineal o ramificado, opcionalmente sustituido por 1 o más halo,  $C_{1-6}$  alcoxil);

$R^p$  es 1, 2, o 3 grupos, seleccionado cada uno independientemente del grupo H, halo, -OH, alquilo de  $C_{1-3}$ ;

$W^3$  se selecciona del grupo de un T-N( $R^{1a}R^{1b}$ ) opcionalmente sustituido, un T-N( $R^{1a}R^{1b}$ ) $X^3$  opcionalmente sustituido, T-Arilo, un T-Heteroarilo opcionalmente sustituido, un T-Heterociclo opcionalmente sustituido, un  $NR^1$ -T-Arilo opcionalmente sustituido, un  $NR^1$ -T-Heteroarilo opcionalmente sustituido o un  $NR^1$ -T-Heterociclo opcionalmente sustituido;

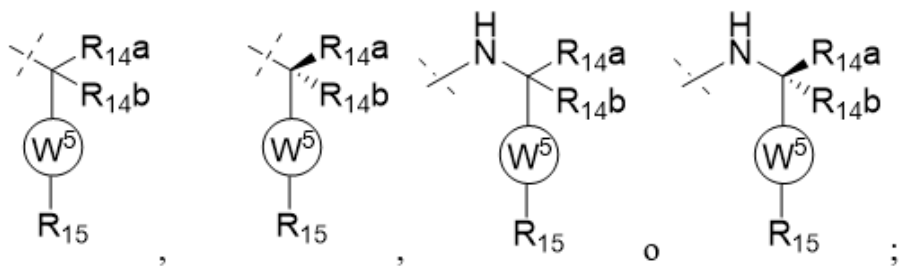
$X^3$  es C=O,  $R^1$ ,  $R^{1a}$ ,  $R^{1b}$ ;

$R^1, R^{1a}, R^{1b}$  se seleccionan cada uno independientemente del grupo que consiste en H, grupo alquilo de  $C_1$ - $C_6$  lineal o ramificado opcionalmente sustituido por 1 o más halo o grupos -OH,  $R^{Y3}C=O$ ,  $R^{Y3}C=S$ ,  $R^{Y3}SO$ ,  $R^{Y3}SO_2$ ,  $N(R^{Y3}R^{Y4})C=O$ ,  $N(R^{Y3}R^{Y4})C=S$ ,  $N(R^{Y3}R^{Y4})SO$ , y  $N(R^{Y3}R^{Y4})SO_2$ ;

T se selecciona del grupo de un alquilo opcionalmente sustituido, grupo  $(CH_2)_n$ , en donde cada uno de los grupos metilenos se sustituye opcionalmente con uno o dos sustituyentes seleccionados del grupo que consiste en halógeno, metilo, un grupo alquilo de  $C_1$ - $C_6$  lineal o ramificado opcionalmente sustituido por 1 o más grupos halógeno u -OH o una cadena lateral de aminoácido opcionalmente sustituido;

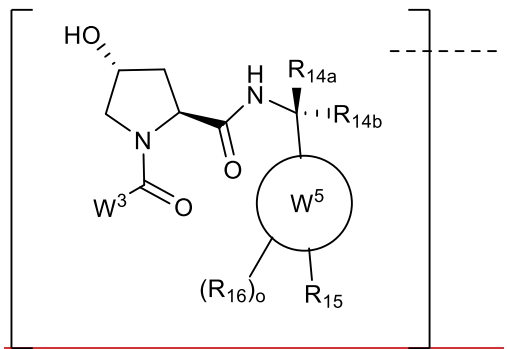
n es 0 a 6;

$W^4$  es



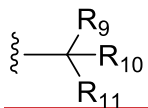
~~R<sub>14a</sub>, R<sub>14b</sub>, se seleccionan cada uno independientemente del grupo que consiste en H, haloalquilo, o alquilo opcionalmente sustituido;~~  
~~W<sup>5</sup> se selecciona del grupo que consiste en un fenilo o un heteroarilo de 5-10 miembros; y~~  
~~R<sub>15</sub> se selecciona del grupo que consiste en H, halógeno, CN, OH, NO<sub>2</sub>, N-R<sub>14a</sub>-R<sub>14b</sub>, OR<sub>14a</sub>, CONR<sub>14a</sub>-R<sub>14b</sub>, NR<sub>14a</sub>-COR<sub>14b</sub>, SO<sub>2</sub>-NR<sub>14a</sub>-R<sub>14b</sub>, NR<sub>14a</sub>-SO<sub>2</sub>-R<sub>14b</sub>, alquilo opcionalmente sustituido, haloalquilo opcionalmente sustituido, haloalcoxi opcionalmente sustituido; arilo, heteroarilo, cicloalquilo, o cicloheteroalquilo,~~  
~~en donde la línea discontinua indica el punto de acoplamiento de al menos una PTM, otra ULM (ULM') o una porción de enlazador químico que acopla al menos una PTM o una ULM' o ambas a la ULM.~~

12. ~~El compuesto de conformidad con cualquiera de las reivindicaciones 1-11, en donde ULM es una porción de unión a la ligasa (VLM) Von Hippel-Lindau (VHL) representada por la estructura:~~

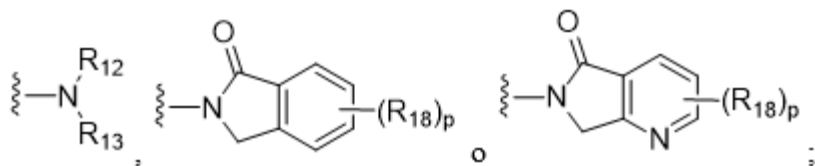


en donde:

~~W<sup>3</sup> se selecciona del grupo que consiste en un arilo opcionalmente sustituido, heteroarilo opcionalmente sustituido, o~~



~~R<sub>9</sub> y R<sub>10</sub> son independientemente hidrógeno, alquilo opcionalmente sustituido, cicloalquilo opcionalmente sustituido, hidroxialquilo opcionalmente sustituido, heteroarilo opcionalmente sustituido, o haloalquilo, o R<sub>9</sub>, R<sub>10</sub>, y el átomo de carbono al que se unen forman un cicloalquilo opcionalmente sustituido;~~  
~~R<sub>11</sub> se selecciona del grupo que consiste en un heterocíclico opcionalmente sustituido, alcoxi opcionalmente sustituido, heteroarilo opcionalmente sustituido, arilo opcionalmente sustituido,~~



~~R<sub>12</sub> se selecciona del grupo que consiste en H o alquilo opcionalmente sustituido;~~

~~R<sub>13</sub> se selecciona del grupo que consiste en H, alquilo opcionalmente sustituido, alquilcarbonilo opcionalmente sustituido, (cicloalquil)alquilcarbonilo opcionalmente sustituido, aralquilcarbonilo opcionalmente sustituido, arilcarbonilo opcionalmente sustituido, (heterocicli)carbonilo opcionalmente sustituido, o aralquilo opcionalmente sustituido;~~

~~R<sub>14a</sub>, R<sub>14b</sub> se seleccionan cada uno independientemente del grupo que consiste en H, haloalquilo, o alquilo opcionalmente sustituido;~~

~~W<sup>5</sup> se selecciona del grupo que consiste en un fenilo o un heteroarilo de 5-10 miembros;~~

~~R<sub>15</sub> se selecciona del grupo que consiste en H, halógeno, CN, OH, NO<sub>2</sub>, N R<sub>14a</sub> R<sub>14b</sub>, OR<sub>14a</sub>, CONR<sub>14a</sub> R<sub>14b</sub>, NR<sub>14a</sub> COR<sub>14b</sub>, SO<sub>2</sub>NR<sub>14a</sub> R<sub>14b</sub>, NR<sub>14a</sub> SO<sub>2</sub> R<sub>14b</sub>, alquilo opcionalmente sustituido, haloalquilo opcionalmente sustituido, haloalcoxi opcionalmente sustituido; arilo, heteroarilo, cicloalquilo, o cicloheteroalquilo (cada uno opcionalmente sustituido independientemente);~~

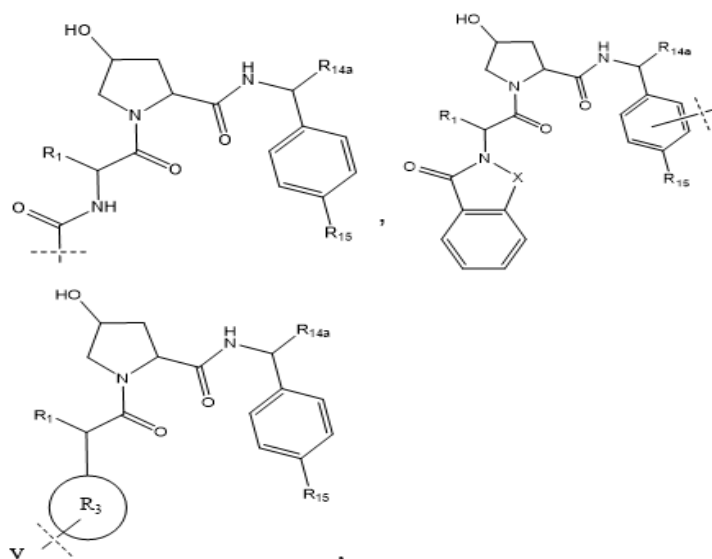
~~R<sub>16</sub> se selecciona independientemente del grupo que consiste en H, halo, alquilo opcionalmente sustituido, haloalquilo opcionalmente sustituido, hidrox, o haloalcoxi opcionalmente sustituido;~~

~~o es 0, 1, 2, 3, o 4;~~

~~R<sub>18</sub> se selecciona independientemente del grupo que consiste en halo, alcoxi opcionalmente sustituido, ciano, alquilo opcionalmente sustituido, haloalquilo, haloalcoxi o un enlazador; y~~

~~p es 0, 1, 2, 3, o 4, y en donde la línea discontinua indica el punto de acoplamiento de al menos una PTM, otra ULM (ULM') o una porción de enlazador químico que acopla al menos una PTM o una ULM' o ambas a la ULM.~~

13. El compuesto de conformidad con cualquiera de las reivindicaciones 1-12, en donde la ULM tiene una estructura química seleccionada del grupo de:



en donde:

~~R<sub>4</sub> es H, etilo, isopropilo, tert-butilo, sec-butilo, ciclopropilo, ciclobutilo, ciclopentilo, o ciclohexilo; alquilo opcionalmente sustituido, hidroxialquilo opcionalmente sustituido, heteroarilo opcionalmente sustituido, o haloalquilo;~~

~~R<sub>14a</sub> es H, haloalquilo, alquilo opcionalmente sustituido, metilo, fluorometilo, hidroximetilo, etilo, isopropilo, o ciclopropilo;~~

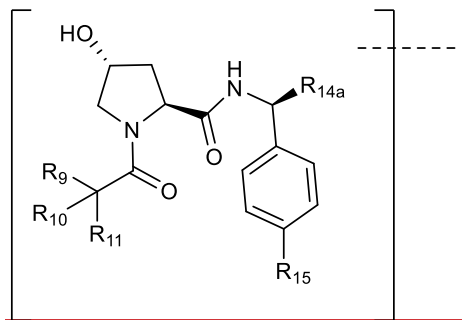
~~R<sub>15</sub> se selecciona del grupo que consiste en H, halógeno, CN, OH, NO<sub>2</sub>, heteroarilo opcionalmente sustituido, arilo opcionalmente sustituido; alquilo opcionalmente sustituido, haloalquilo opcionalmente sustituido, haloalcoxi opcionalmente sustituido, cicloalquilo, o cicloheteroalquilo;~~

~~X es C, CH<sub>2</sub>, o C=O; y~~

~~R<sub>3</sub> es un enlace o un heteroarilo de 5 o 6 miembros opcionalmente sustituido,~~

~~en donde la línea discontinua indica el punto de acoplamiento de al menos una PTM, otra ULM (ULM') o una porción de enlazador químico que acopla al menos una PTM o una ULM' o ambas a la ULM.~~

14.—El compuesto de conformidad con cualquiera de las reivindicaciones 1-13, en donde la ULM comprende un grupo de conformidad con la estructura química:



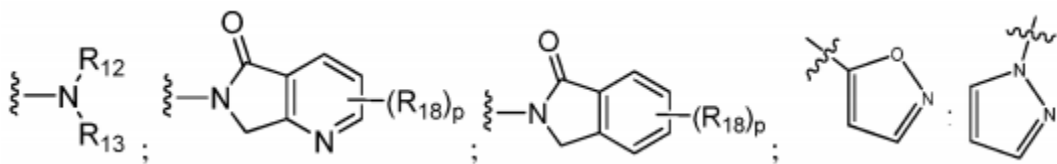
en donde:

~~R<sub>14a</sub> es H, haloalquilo, alquilo opcionalmente sustituido, metilo, fluorometilo, hidroximetilo, etilo, isopropilo, o ciclopropilo;~~

~~R<sub>9</sub> es H;~~

~~R<sub>10</sub> es H, etilo, isopropilo, tert-butilo, sec-butilo, ciclopropilo, ciclobutilo, ciclopentilo, o ciclohexilo;~~

~~R<sub>11</sub> es~~



~~o heteroarilo opcionalmente sustituido;~~

~~p es 0, 1, 2, 3, o 4;~~

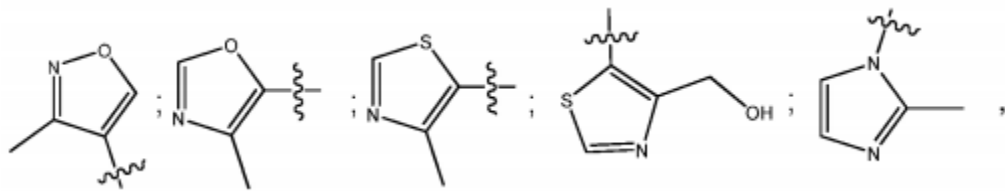
~~cada R<sub>18</sub> es independientemente halo, alcoxi opcionalmente sustituido, ciano, alquilo opcionalmente sustituido, haloalquilo, haloalcoxi o un enlazador;~~

~~R<sub>12</sub> es H, C=O;~~

~~R<sub>13</sub> es H, alquilo opcionalmente sustituido, alquilcarbonilo opcionalmente sustituido, (cicloalquil)alquilcarbonilo opcionalmente sustituido, aralquilcarbonilo opcionalmente sustituido,~~

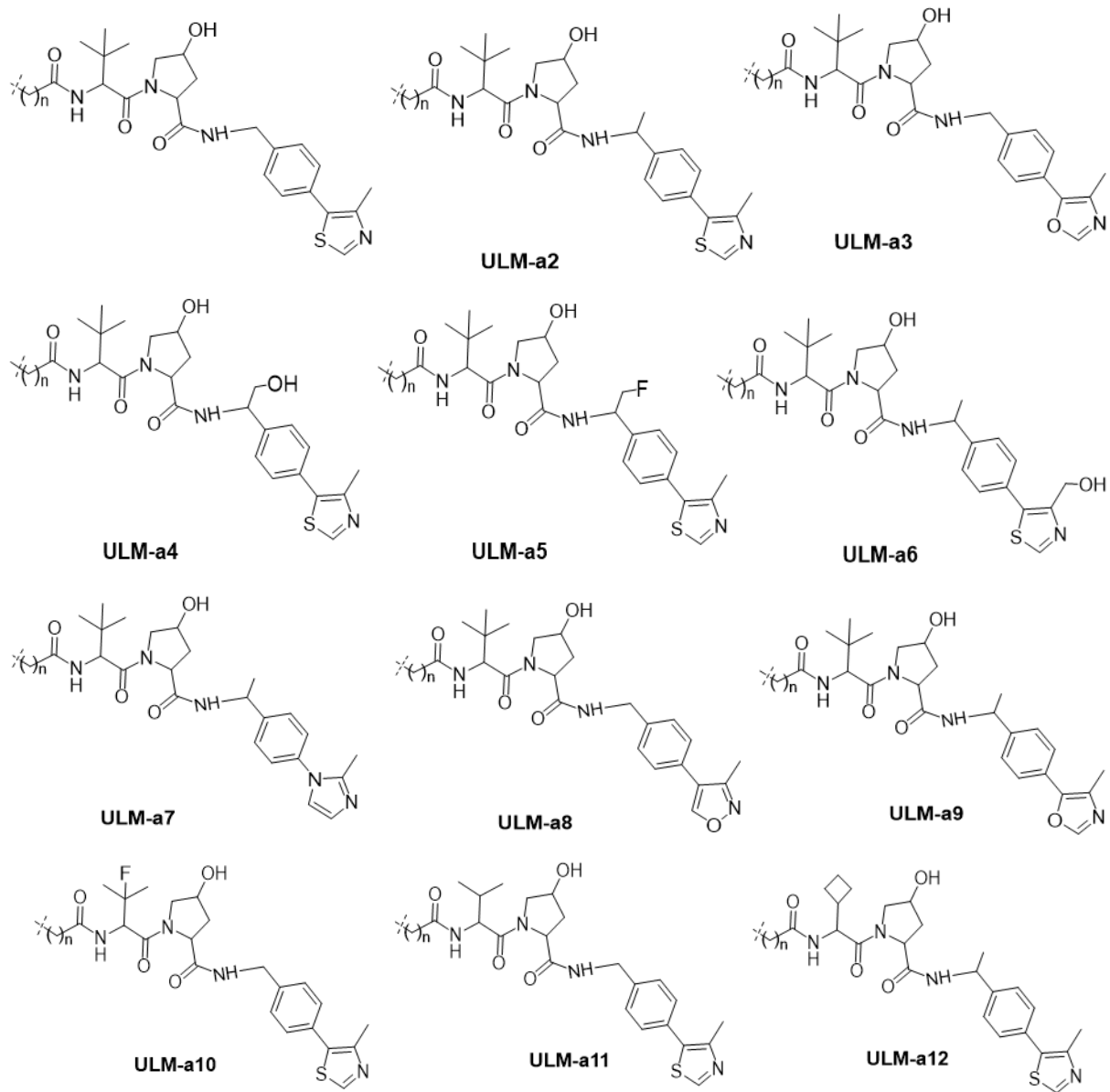
~~arilcarbonilo opcionalmente sustituido, (heterocicli)carbonilo opcionalmente sustituido, o aralquilo opcionalmente sustituido; y~~

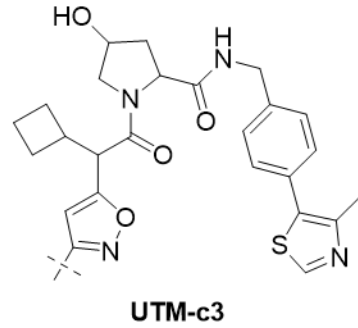
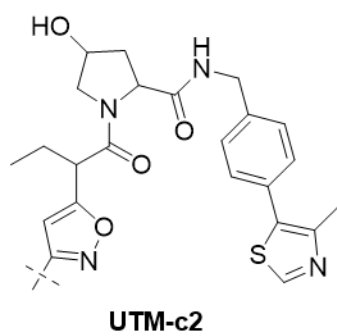
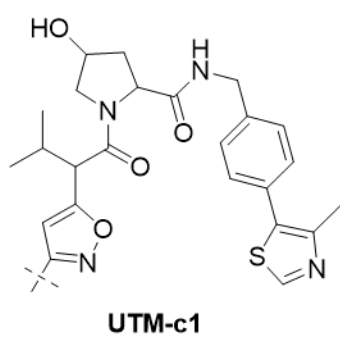
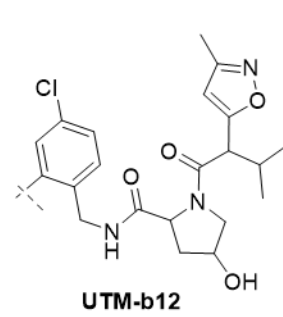
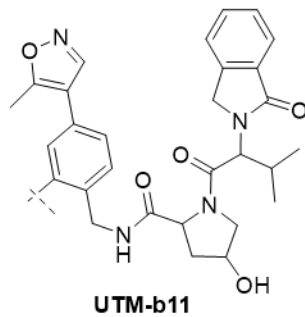
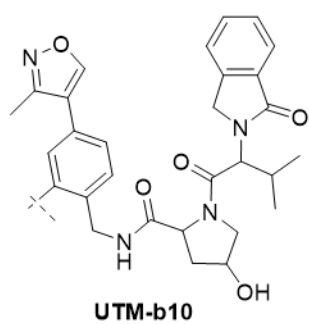
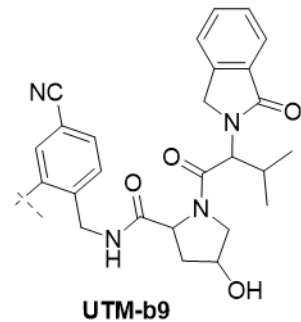
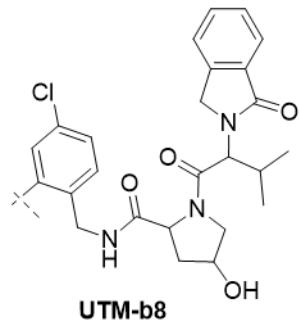
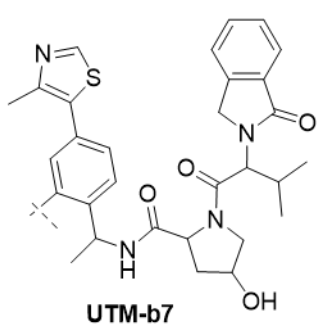
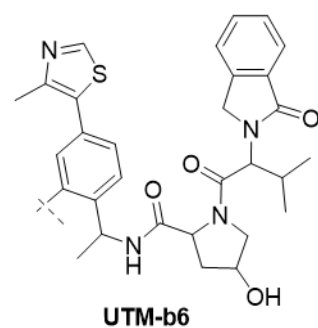
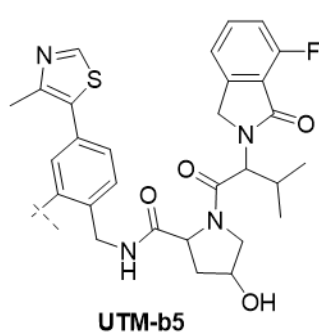
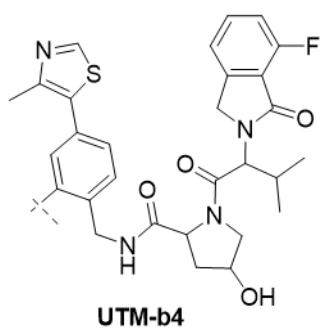
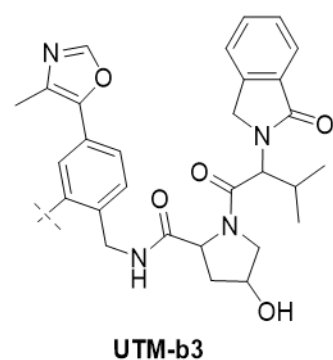
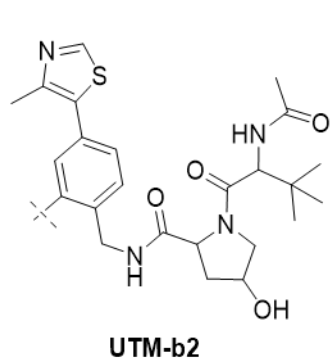
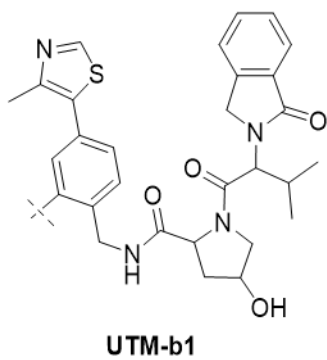
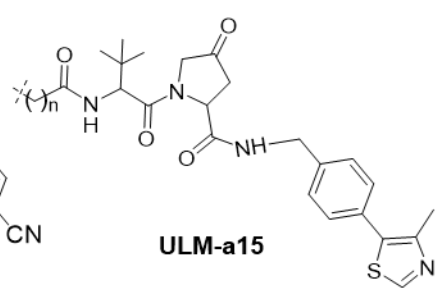
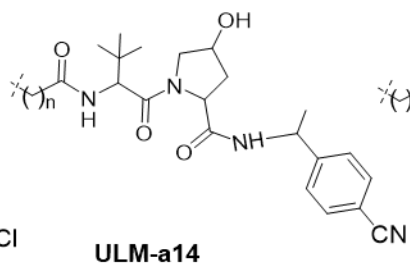
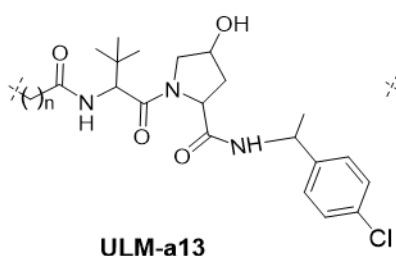
~~R<sub>15</sub> se selecciona del grupo que consiste en H, halógeno, Cl, CN, OH, NO<sub>2</sub>, heteroarilo opcionalmente sustituido, arilo opcionalmente sustituido;~~

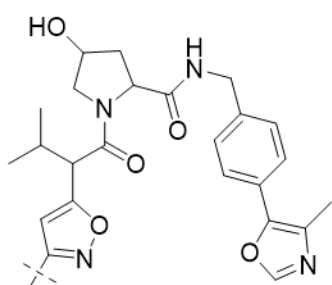


~~en donde la línea discontinua indica el punto de acoplamiento de al menos una PTM, otra ULM (ULM') o una porción de enlazador químico que acopla al menos una PTM o una ULM' o ambas a la ULM.~~

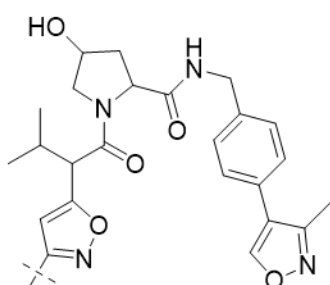
315. El compuesto de conformidad con ~~cualquiera de las reivindicacion~~reivindicaciones 1-14 o reivindicación 2, en donde la ULM comprende un grupo seleccionado de la estructura que consiste en:



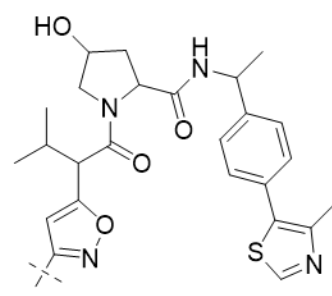




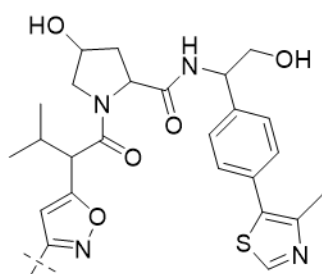
UTM-c4



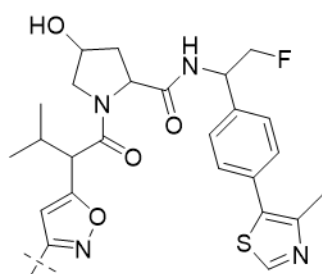
UTM-c5



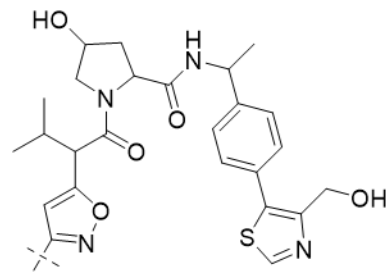
UTM-c6



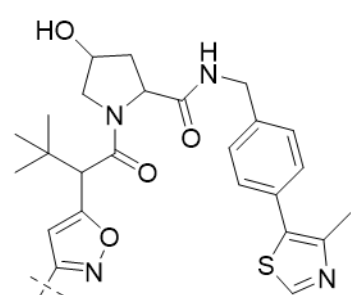
UTM-c7



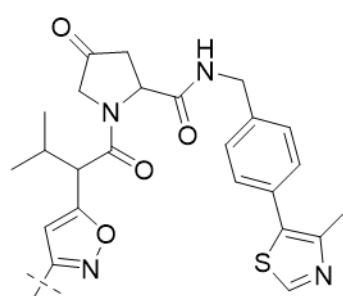
UTM-c8



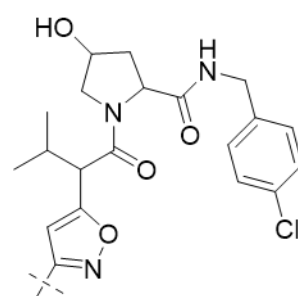
UTM-c9



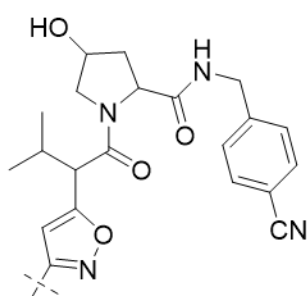
UTM-c10



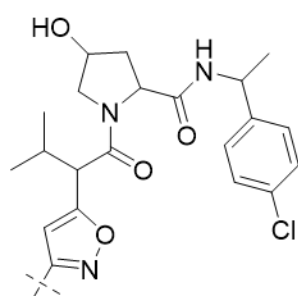
UTM-c11



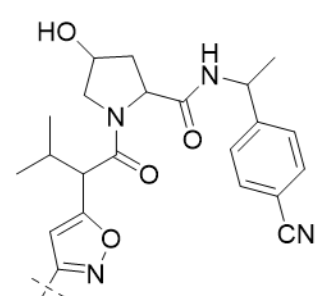
UTM-c12



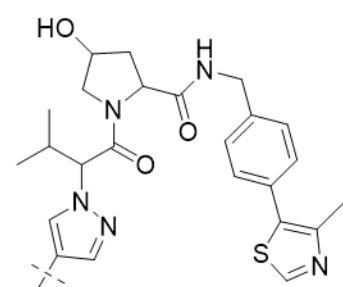
UTM-c13



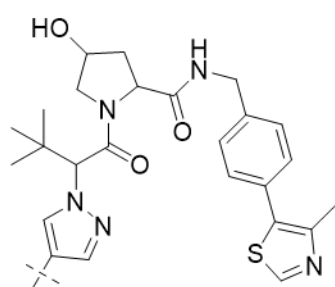
UTM-c14



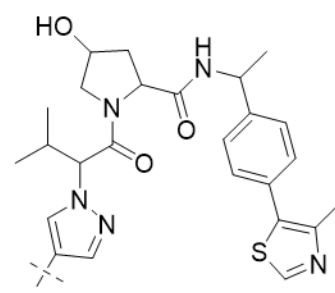
UTM-c15



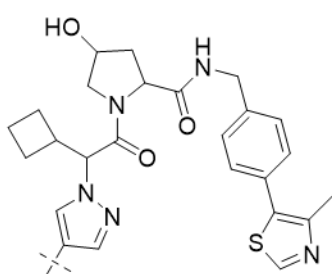
UTM-d1



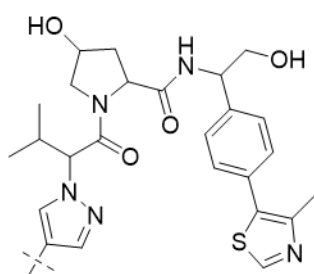
UTM-d2



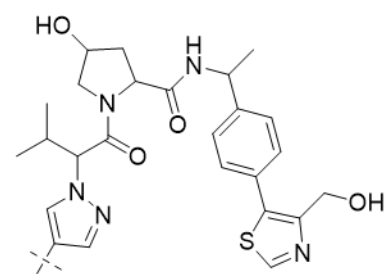
UTM-d3



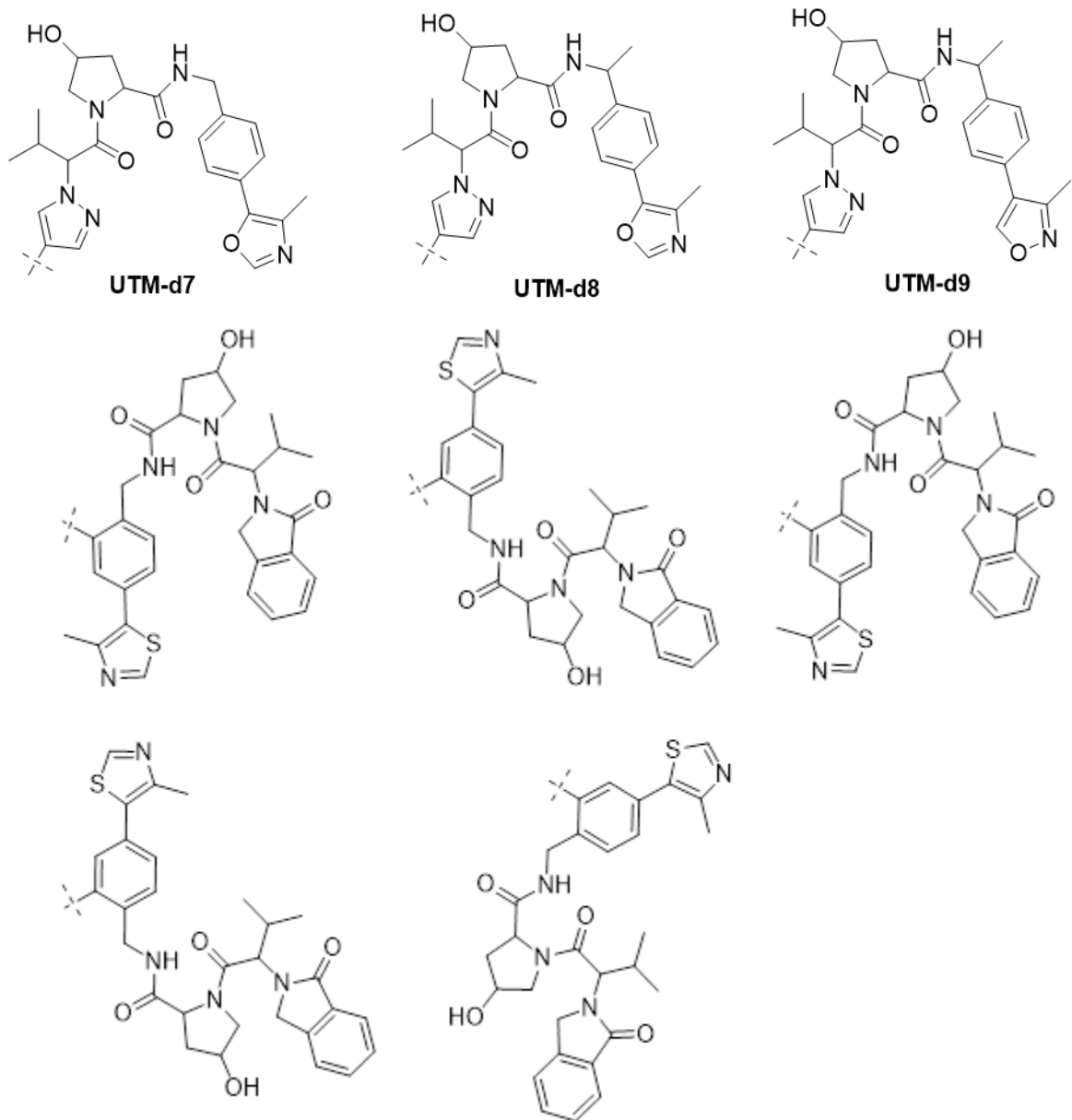
UTM-d4



UTM-d5



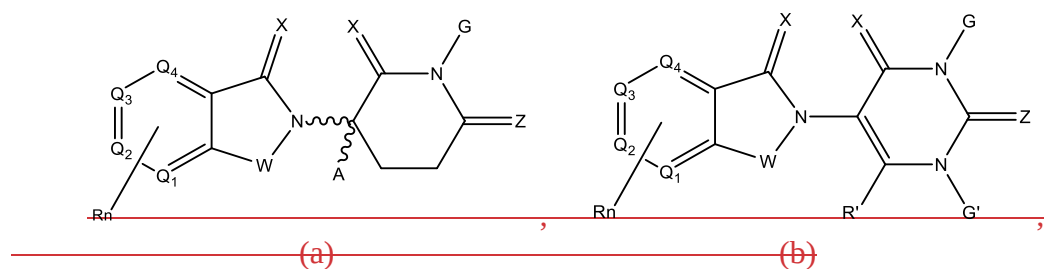
UTM-d6

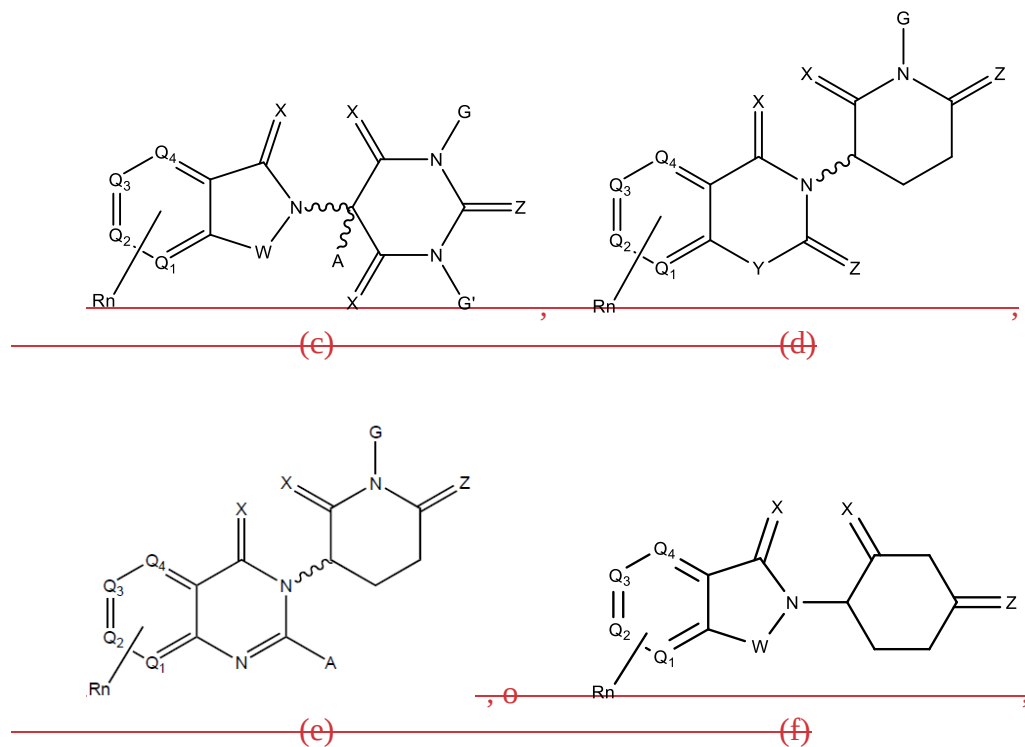


en donde el anillo fenilo en la ULM-a1 hasta la ULM-a15, ULM-b1 hasta la ULM-b12, ULM-c1 hasta la ULM-c15 y ULM-d1 hasta la ULM-d9 se sustituye opcionalmente con **grupos**-fluor, **alquilo inferior y alcoxi**, y en donde la línea discontinua indica el punto de acoplamiento de **al menos una PTM, otra ULM (ULM') o una** porción de enlazador químico **que acopla al menos una PTM o una ULM' o ambas a la ULM-a**.

16.—El compuesto de conformidad con cualquiera de las reivindicaciones 1-10, en donde la ULM es una porción de unión a la ligasa de ubiquitina E3 cereblon (CLM) seleccionada del grupo que consiste en talidomida, lenalidomida, pomalidomida, sus análogos, sus isoésteres, y sus derivados.

17.—El compuesto de conformidad con cualquiera de las reivindicaciones 1-10, o 16, en donde la CLM tiene una estructura química representada por:





en donde:

~~W se selecciona del grupo que consiste en CH<sub>2</sub>, CHR, C=O, SO<sub>2</sub>, NH, y N alquilo;~~

~~cada X se selecciona independientemente del grupo que consiste en O, S, y H<sub>2</sub>;~~

~~Y se selecciona del grupo que consiste en CH<sub>2</sub>, C=CR', NH, N alquilo, N arilo, N hetarilo, N cicloalquilo, N heterociclilo, O, y S;~~

~~Z se selecciona del grupo que consiste en O, S, y H<sub>2</sub>;~~

~~G y G' se seleccionan independientemente del grupo que consiste en H, alquilo (lineal, ramificado, opcionalmente sustituido con R'), OH, R'OCOOR, R'OCONRR'', CH<sub>2</sub>-heterociclilo opcionalmente sustituido con R', y bencilo opcionalmente sustituido con R';~~

~~Q<sub>1</sub>, Q<sub>2</sub>, Q<sub>3</sub>, y Q<sub>4</sub> representan un carbono C sustituido con un grupo independientemente seleccionado de R', N o N-óxido;~~

~~A se selecciona independientemente del grupo H, alquilo, cicloalquilo, Cl y F;~~

~~R comprende CONR'R'', OR', NR'R'', SR', SO<sub>2</sub>R', SO<sub>2</sub>NR'R'', CR'R'', CR'NR'R'', arilo, hetarilo, alquilo (lineal, ramificado, opcionalmente sustituido), cicloalquilo, heterociclilo, P(O)(OR')R'', P(O)R'R'', OP(O)(OR')R'', OP(O)R'R'', Cl, F, Br, I, CF<sub>3</sub>, CN, NR'SO<sub>2</sub>NR'R'', NR'CONR'R'', CONR'COR'', NR'C(=N-CN)NR'R'', C(=N-CN)NR'R'', NR'C(=N-CN)R'', NR'C(=C-NO<sub>2</sub>)NR'R'', SO<sub>2</sub>NR'COR'', NO<sub>2</sub>, CO<sub>2</sub>R', C(C=N OR')R'', CR'=CR'R'', CCR', S(C=O)(C=N-R')R'', SF<sub>5</sub> o OCF<sub>3</sub>;~~

~~R' y R'' se seleccionan independientemente del grupo que consiste en un enlace, H, N, N-óxido, alquilo (lineal, ramificado), cicloalquilo, arilo, heteroarilo, heterocíclico, C(=O)R, o heterociclilo, cada uno de los cuales es opcionalmente sustituido;~~

~~~~~~~ representa un enlace que puede ser estereoespecífico ((R) o (S)) o no estereoespecífico;~~

~~y~~

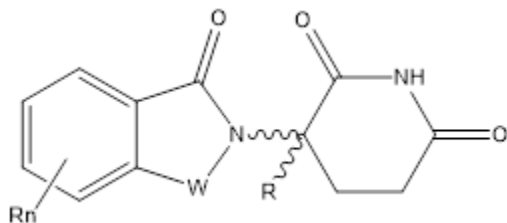
~~R_n comprende un grupo funcional o un átomo,~~

~~en donde n es un número de 1-4, y en donde~~

~~cuando n es 1, R_n se modifica para unirse covalentemente al grupo enlazador (L), y~~

~~cuando n es 2, 3, o 4, entonces una R_n se modifica para unirse covalentemente al grupo enlazador (L), y cualquiera otra R_n se modifica opcionalmente para unirse covalentemente a una PTM, una CLM, una segunda CLM que tiene la misma estructura química que la CLM, una CLM', un segundo enlazador, o cualquier múltiplo o sus combinaciones.~~

184. El compuesto de conformidad con ~~cualquiera de las reivindicaciones~~reivindicación 1-10, 16 o 17reivindicación 2, en donde la CLM tiene una estructura química representada por:



en donde:

W se selecciona independientemente del grupo CH₂, C=O, y NH, ~~y N-alquilo~~;

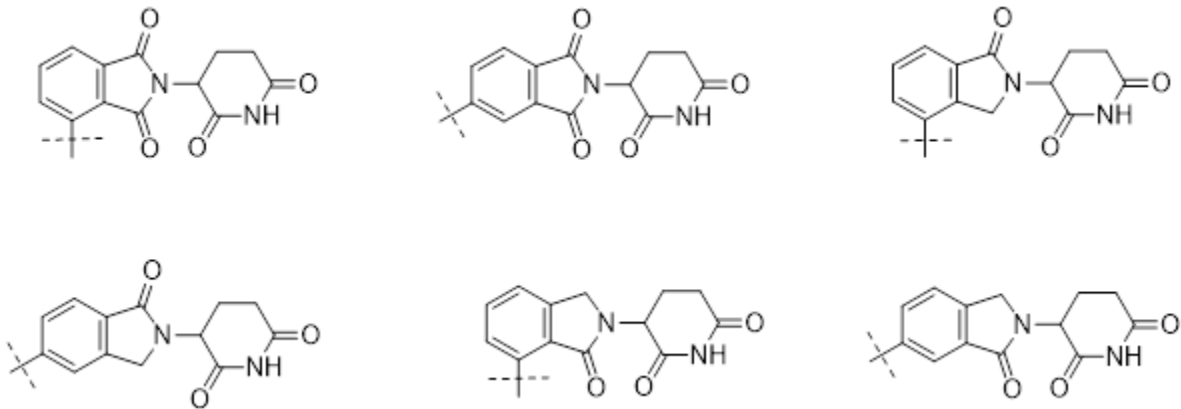
R se selecciona independientemente de un H, metilo, alquilo;

~~~~ representa un enlace que puede ser estereoespecífico ((R) o (S)) o no estereoespecífico;

y

R<sub>n</sub> comprende ~~1-4 grupos funcionales o átomos seleccionados independientemente, y~~  
~~opcionalmente, uno de los cuales se modifica para unirse covalentemente a una PTM,~~ un grupo enlazador químico (L), ~~una CLM (o CLM') o sus combinaciones.~~

195. El compuesto de conformidad con cualquiera de las reivindicaciones ~~1-10, 2,~~ o ~~16-184,~~ en donde la CLM tiene una estructura química representada por:



en donde las líneas discontinuas indican los puntos de acoplamiento del enlazador.

~~20. El compuesto de conformidad con cualquiera de las reivindicaciones 1-19, en donde el enlazador (L) comprende una unidad estructural química representada por la Fórmula:~~



~~en donde:~~

~~A es un grupo que se conecta a la porción ULM o PTM; y~~

~~q es un número mayor que o igual a 1,~~

~~en donde A se selecciona del grupo que consiste en, un enlace, CR<sup>L1</sup>R<sup>L2</sup>, O, S, SO, SO<sub>2</sub>, NR<sup>L3</sup>, SO<sub>2</sub>NR<sup>L3</sup>, SONR<sup>L3</sup>, CONR<sup>L3</sup>, NR<sup>L3</sup>CONR<sup>L4</sup>, NR<sup>L3</sup>SO<sub>2</sub>NR<sup>L4</sup>, CO, CR<sup>L1</sup>=CR<sup>L2</sup>, C≡C,~~

~~SiR<sup>L1</sup>R<sup>L2</sup>, P(O)R<sup>L1</sup>, P(O)OR<sup>L1</sup>, NR<sup>L3</sup>C(=NCN)NR<sup>L4</sup>, NR<sup>L3</sup>C(=NCN), NR<sup>L3</sup>C(=CNO<sub>2</sub>)NR<sup>L4</sup>, cicloalquilo de C<sub>3-11</sub> opcionalmente sustituido con grupos 0-6 R<sup>L1</sup> y/o R<sup>L2</sup>, heterociclilo de C<sub>3-11</sub> opcionalmente sustituido con grupos 0-6 R<sup>L1</sup> y/o R<sup>L2</sup>, arilo opcionalmente sustituido con grupos 0-6 R<sup>L1</sup> y/o R<sup>L2</sup>, heteroarilo opcionalmente sustituido con grupos 0-6 R<sup>L1</sup> y/o R<sup>L2</sup>, donde R<sup>L1</sup> o R<sup>L2</sup>, cada uno independientemente se unen opcionalmente a otros grupos para formar porciones cicloalquilo y/o heterociclilo, opcionalmente sustituidos con grupos 0-4 R<sup>L5</sup>;~~

~~R<sup>L1</sup>, R<sup>L2</sup>, R<sup>L3</sup>, R<sup>L4</sup> y R<sup>L5</sup> son, cada uno independientemente, H, halo, alquilo de C<sub>1-8</sub>, OC<sub>1-8</sub>alquilo, SC<sub>1-8</sub>alquilo, NHC<sub>1-8</sub>alquilo, N(C<sub>1-8</sub>alquilo)<sub>2</sub>, C<sub>3-11</sub>cicloalquilo, arilo, heteroarilo, C<sub>3-11</sub>heterociclilo, OC<sub>1-8</sub>cicloalquilo, SC<sub>1-8</sub>cicloalquilo, NHC<sub>1-8</sub>cicloalquilo, N(C<sub>1-8</sub>cicloalquilo)<sub>2</sub>, N(C<sub>1-8</sub>cicloalquilo)(C<sub>1-8</sub>alquilo), OH, NH<sub>2</sub>, SH, SO<sub>2</sub>C<sub>1-8</sub>alquilo, P(O)(OC<sub>1-8</sub>alquilo)(C<sub>1-8</sub>alquilo), P(O)(OC<sub>1-8</sub>alquilo)<sub>2</sub>, CC<sub>1-8</sub>alquilo, CCH, CH=CH(C<sub>1-8</sub>alquilo), C(C<sub>1-8</sub>alquilo)=CH(C<sub>1-8</sub>alquilo), C(C<sub>1-8</sub>alquilo)=C(C<sub>1-8</sub>alquilo)<sub>2</sub>, Si(OH)<sub>3</sub>, Si(C<sub>1-8</sub>alquilo)<sub>3</sub>, Si(OH)(C<sub>1-8</sub>alquilo)<sub>2</sub>, COC<sub>1-8</sub>alquilo, CO<sub>2</sub>H, halógeno, CN, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, NO<sub>2</sub>, SF<sub>5</sub>, SO<sub>2</sub>NHC<sub>1-8</sub>alquilo, SO<sub>2</sub>N(C<sub>1-8</sub>alquilo)<sub>2</sub>, SONHC<sub>1-8</sub>alquilo, SON(C<sub>1-8</sub>alquilo)<sub>2</sub>, CONHC<sub>1-8</sub>alquilo, CON(C<sub>1-8</sub>alquilo)<sub>2</sub>, N(C<sub>1-8</sub>alquilo)CONH(C<sub>1-8</sub>alquilo), N(C<sub>1-8</sub>alquilo)CON(C<sub>1-8</sub>alquilo)<sub>2</sub>, NHCONH(C<sub>1-8</sub>alquilo), NHCON(C<sub>1-8</sub>alquilo)<sub>2</sub>, NHCONH<sub>2</sub>, N(C<sub>1-8</sub>alquilo)SO<sub>2</sub>NH(C<sub>1-8</sub>alquilo), N(C<sub>1-8</sub>alquilo)SO<sub>2</sub>N(C<sub>1-8</sub>alquilo)<sub>2</sub>, NH SO<sub>2</sub>NH(C<sub>1-8</sub>alquilo), NH SO<sub>2</sub>N(C<sub>1-8</sub>alquilo)<sub>2</sub>, NH SO<sub>2</sub>NH<sub>2</sub>;~~

**216.** El compuesto de conformidad con cualquiera de las reivindicaciones 1-~~20~~ a 5, en donde el enlazador (L) comprende un grupo representado por una estructura general seleccionada del grupo que consiste en:

-N(R)-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-OCH<sub>2</sub>-,

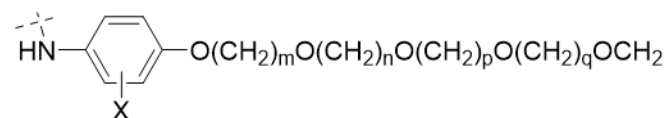
-O-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-OCH<sub>2</sub>-,

-O-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-O-;

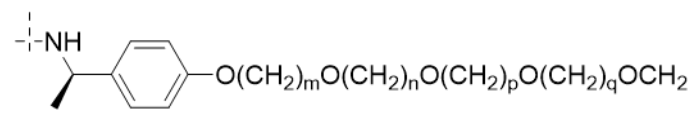
-N(R)-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-O-;

-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-O-;

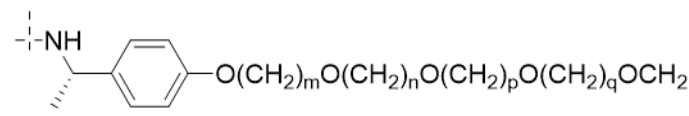
-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-OCH<sub>2</sub>-;



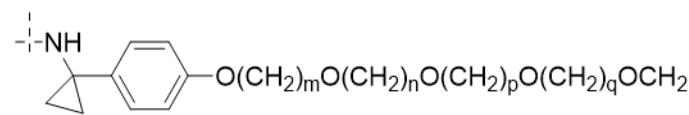
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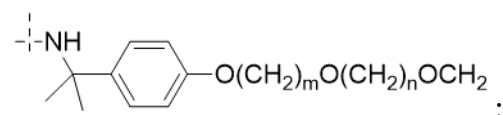
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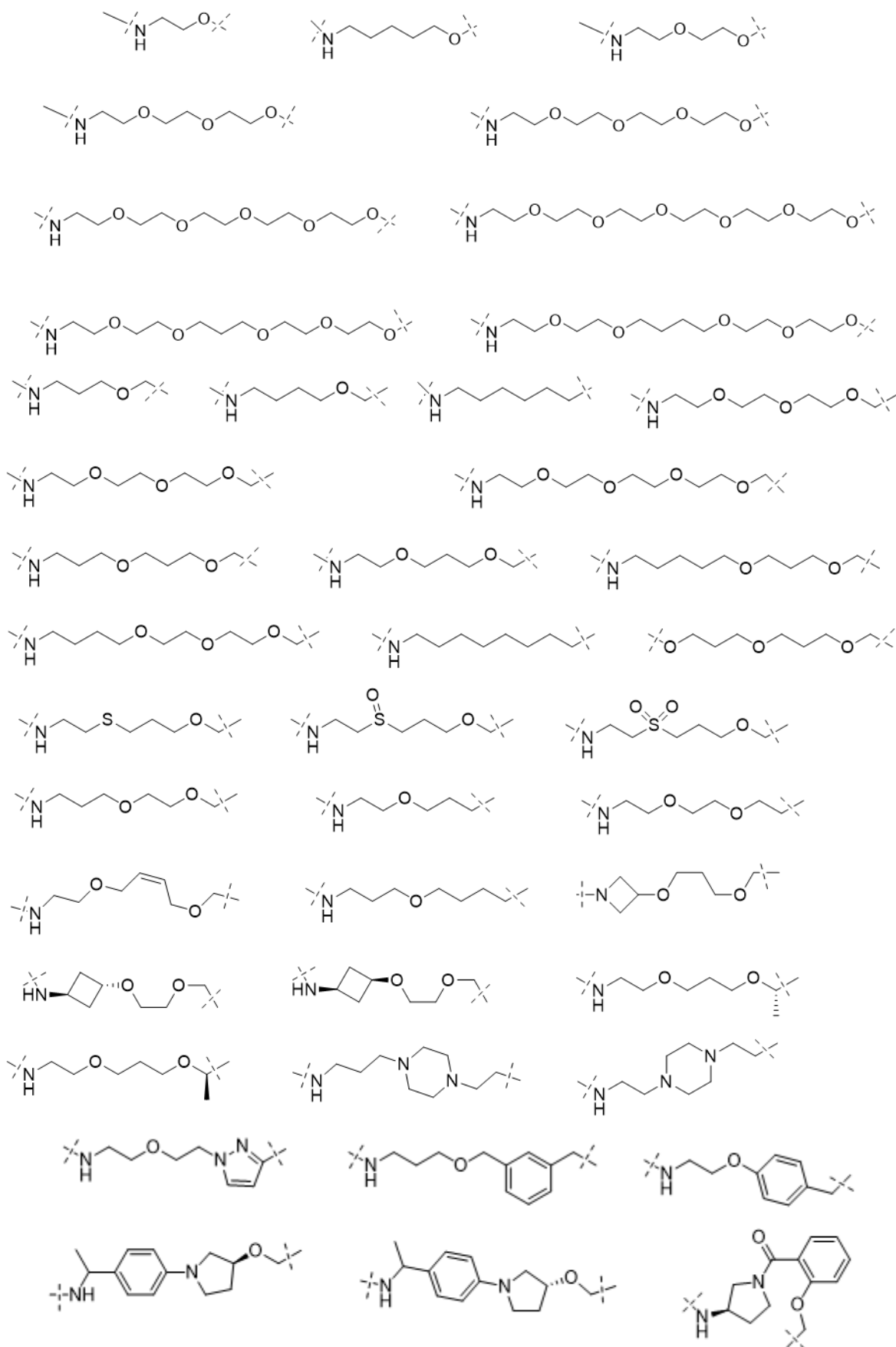
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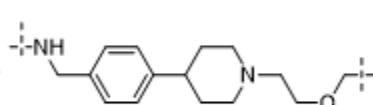
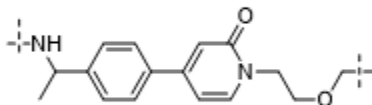
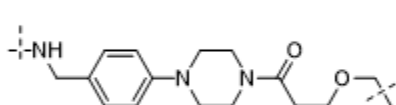
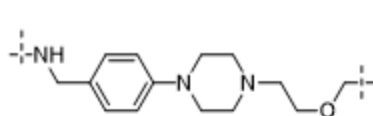
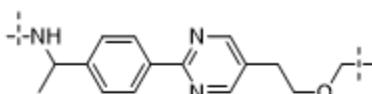
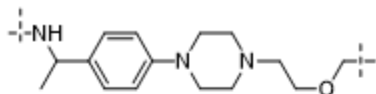
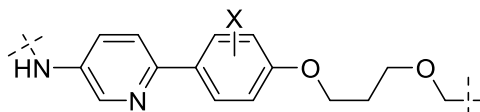
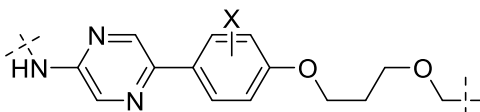
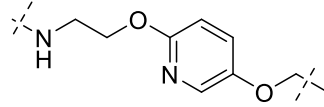
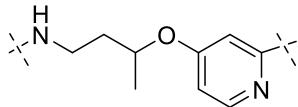
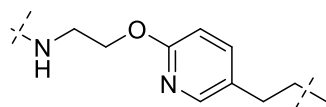
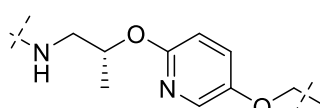
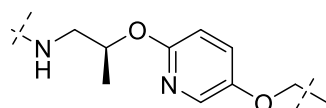
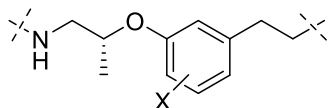
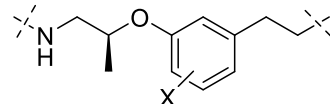
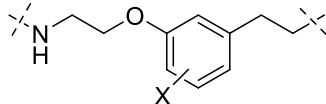
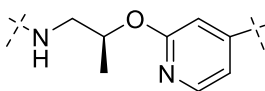
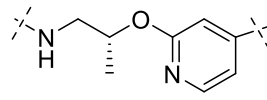
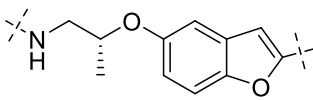
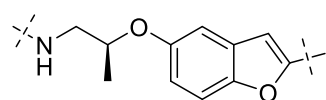
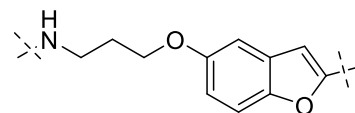
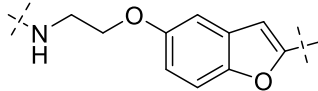
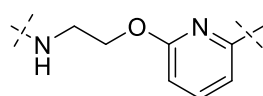
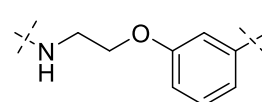
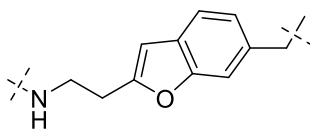
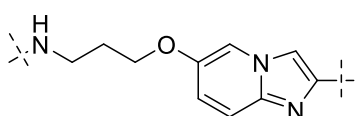
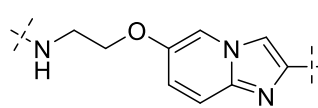
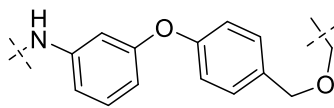
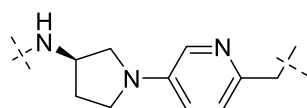
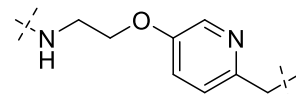
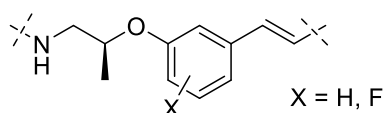
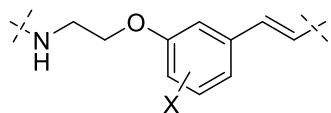
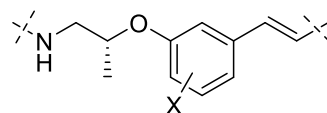
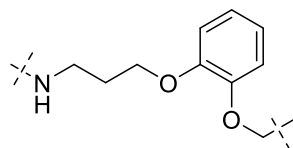
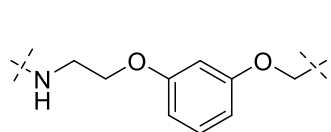
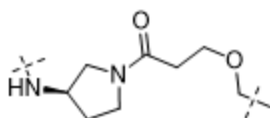
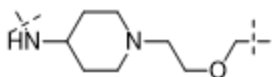
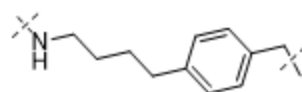
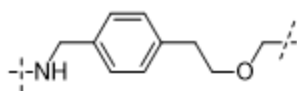
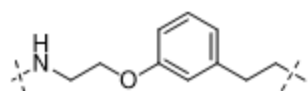


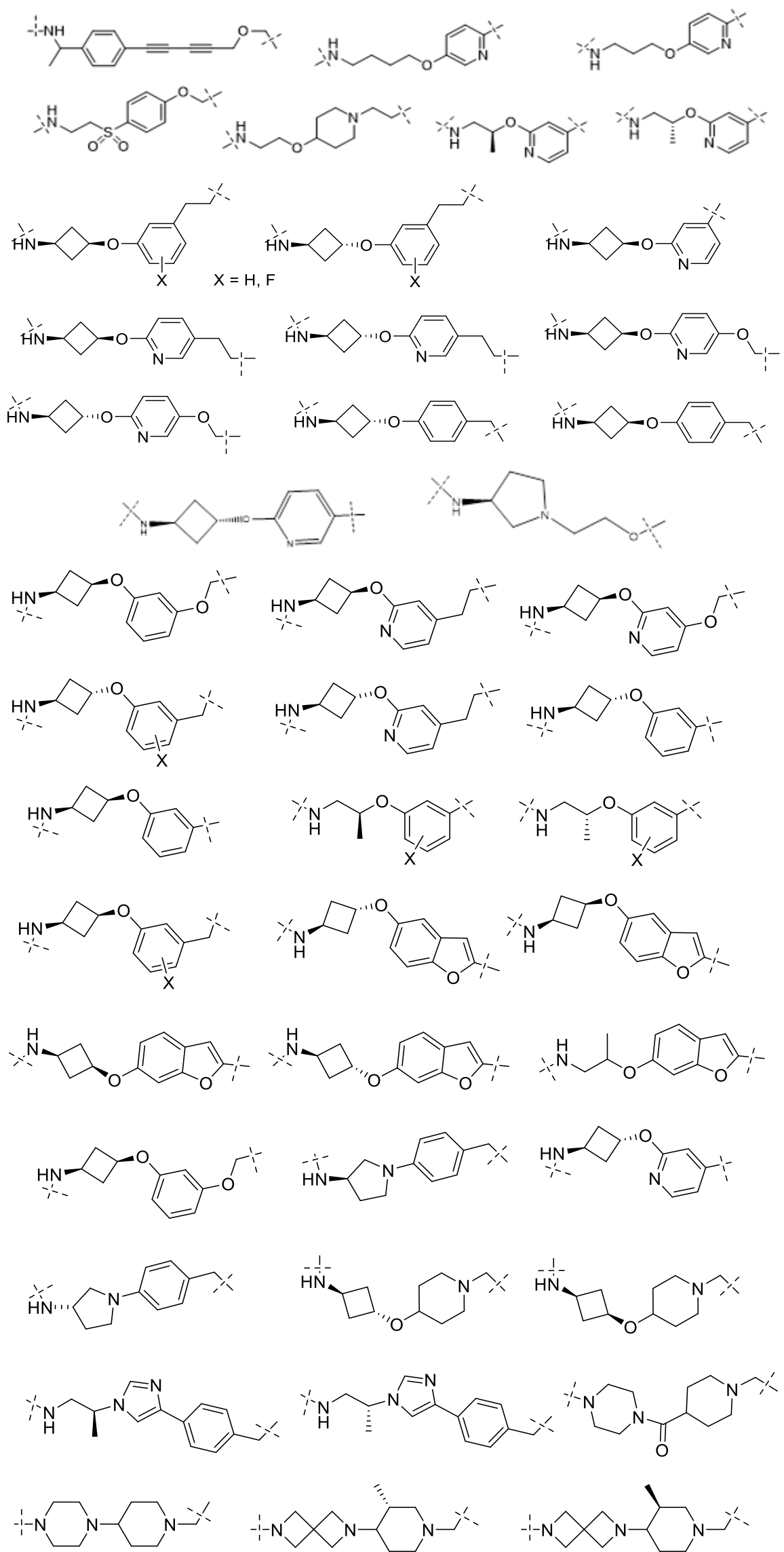
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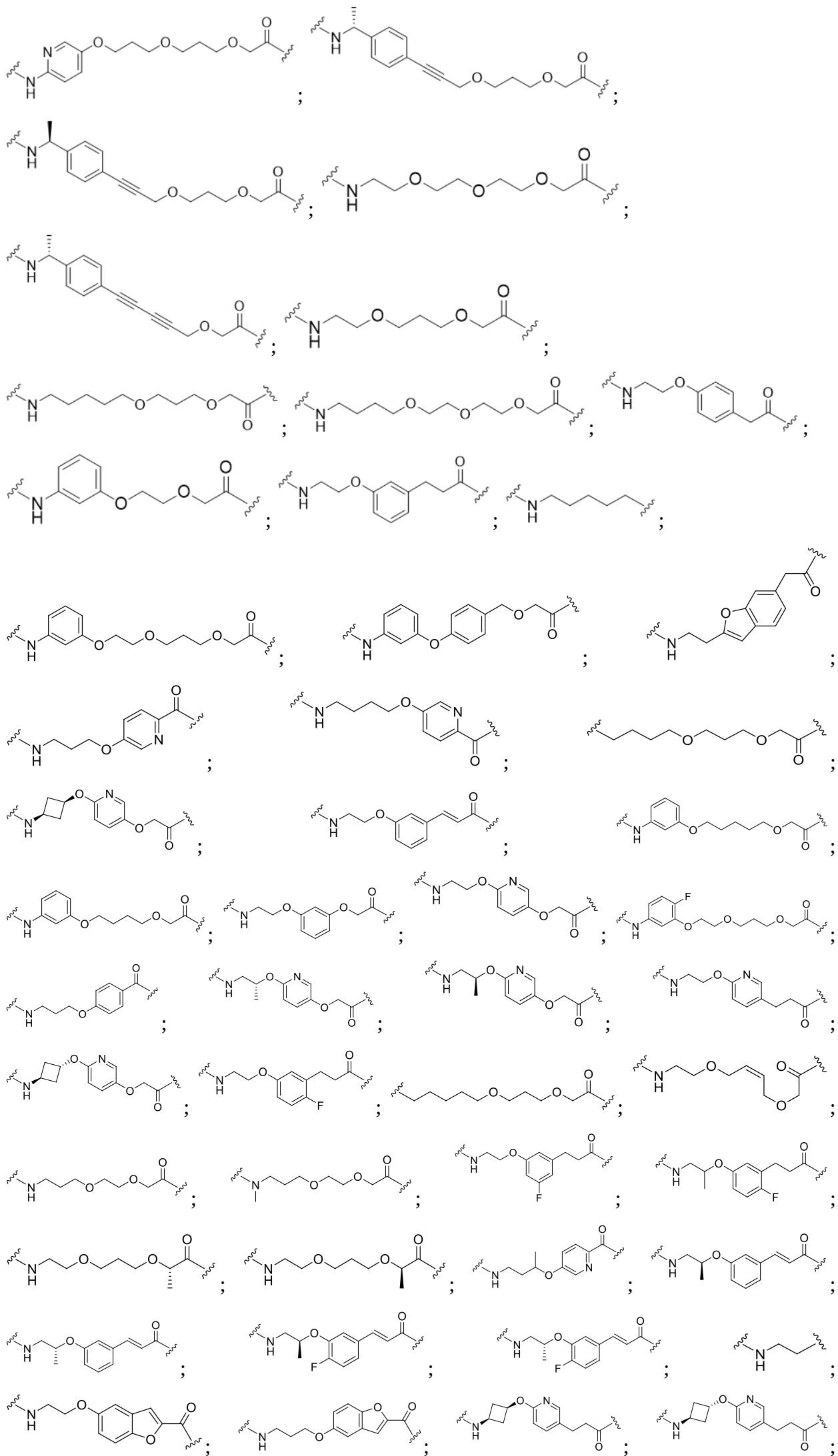
y  $X$  se selecciona del grupo  $H$  o  $F$ ;

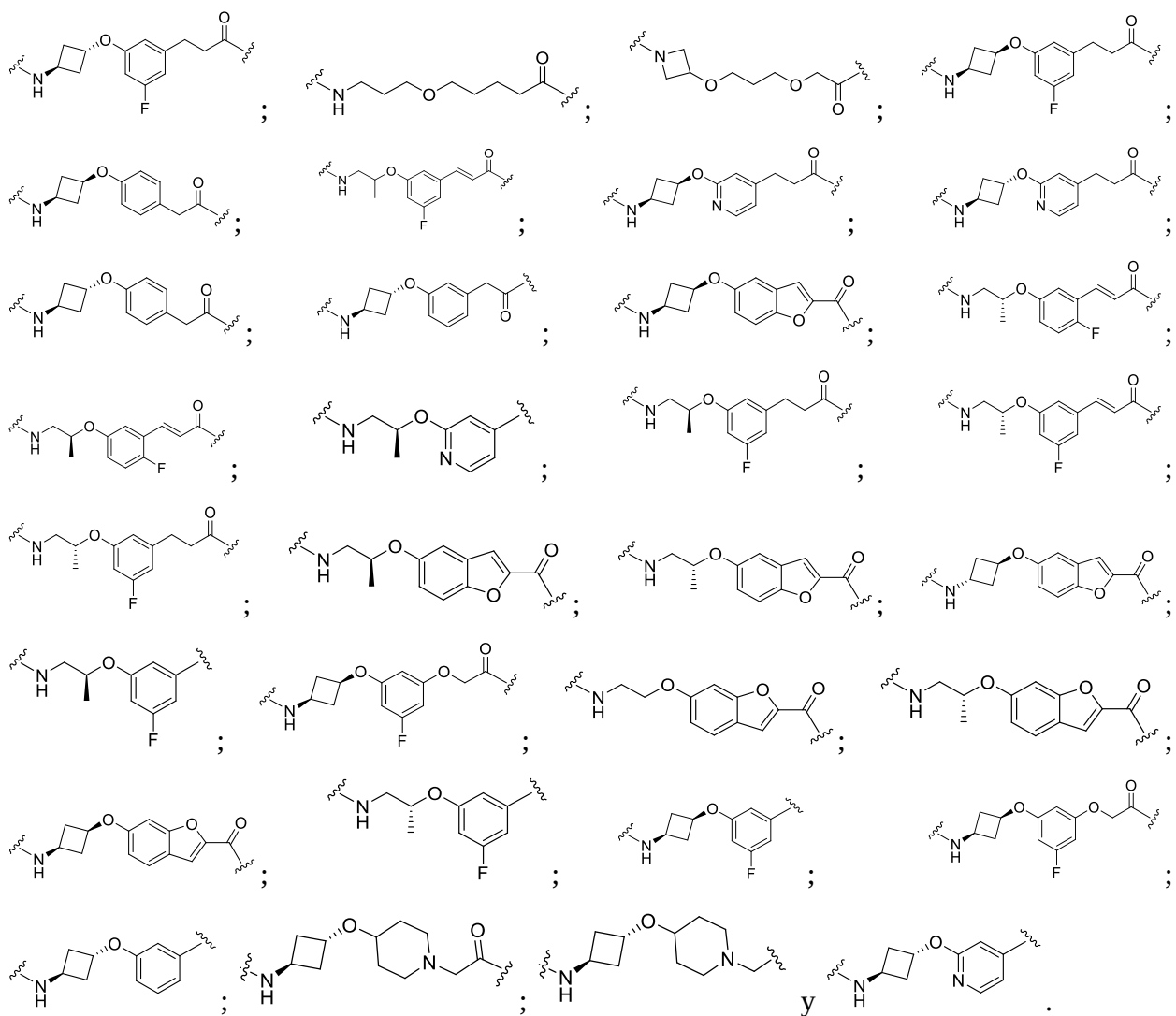




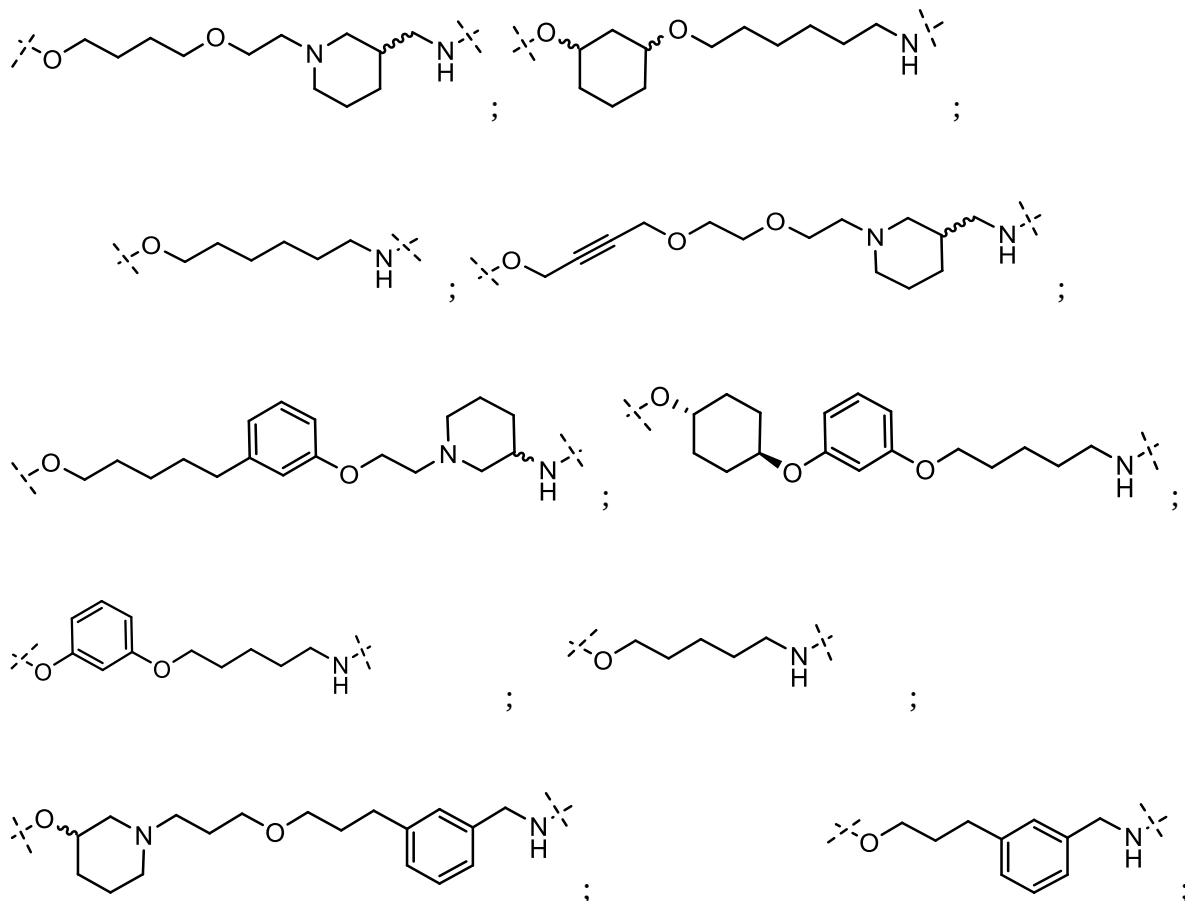


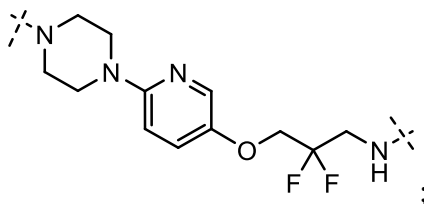
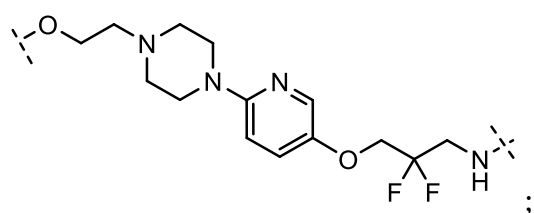
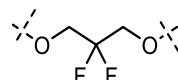
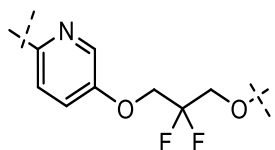
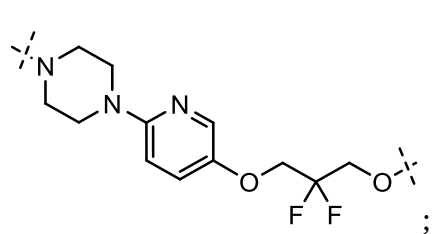
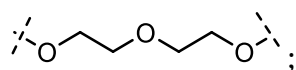
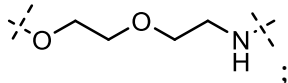
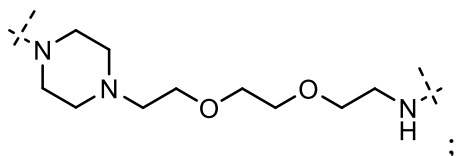
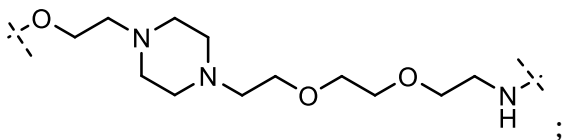
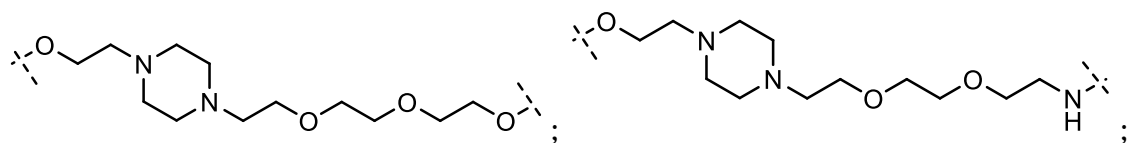
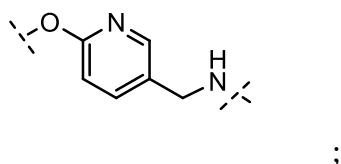
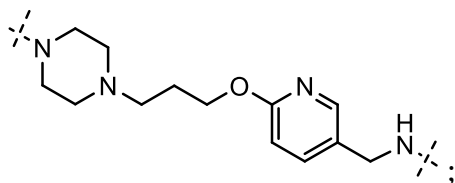
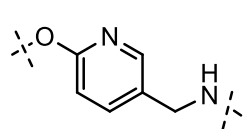
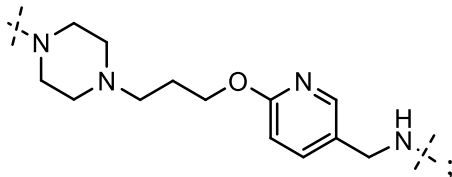
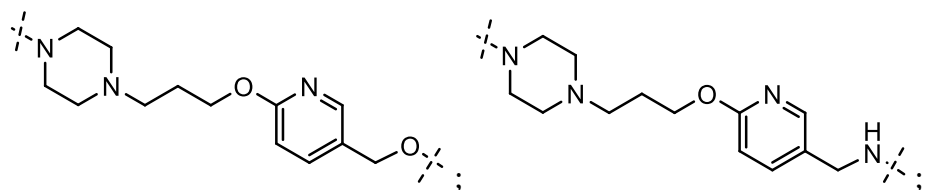
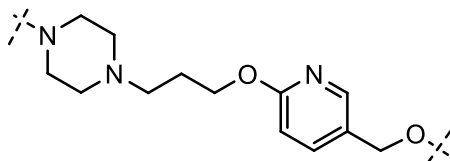
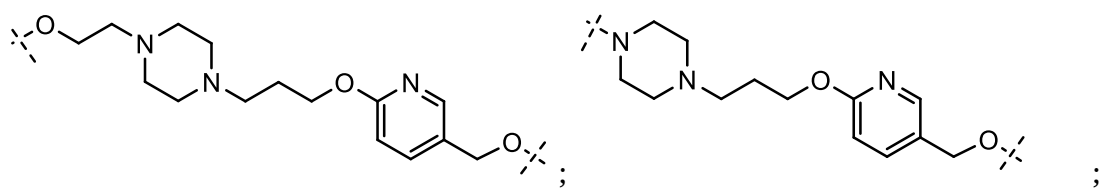
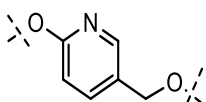
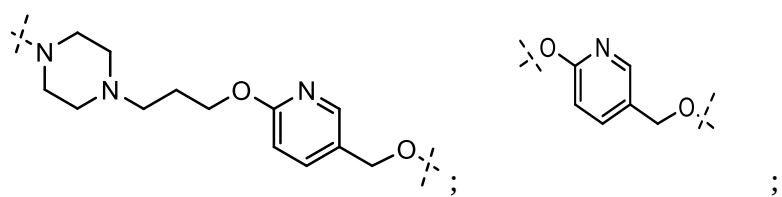


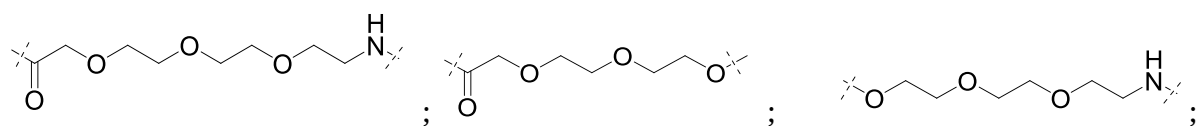
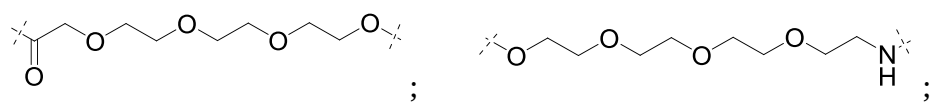
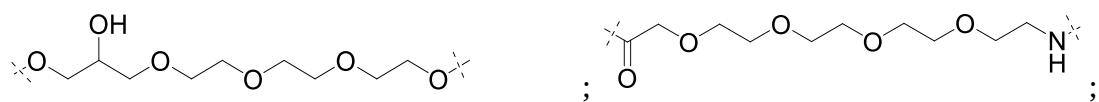
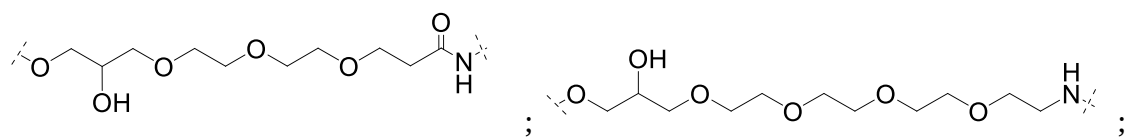
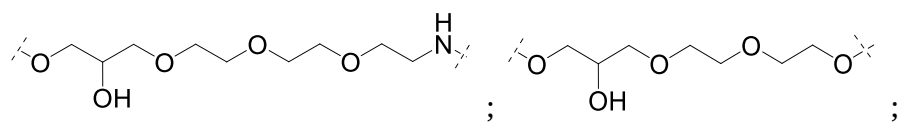
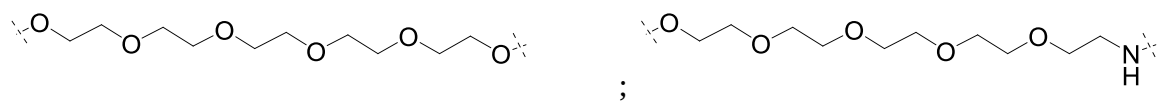
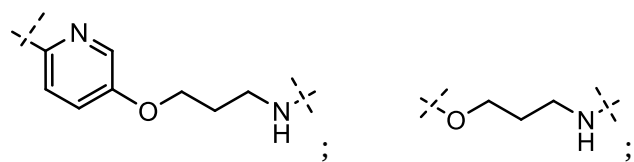
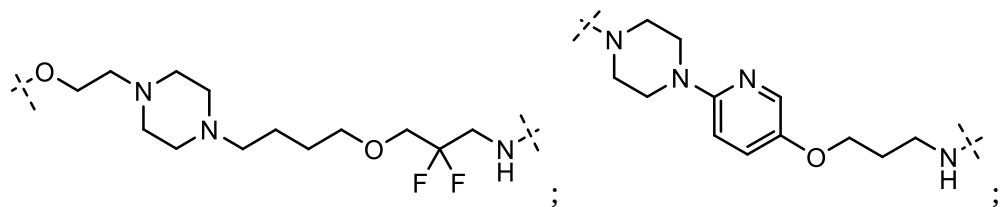
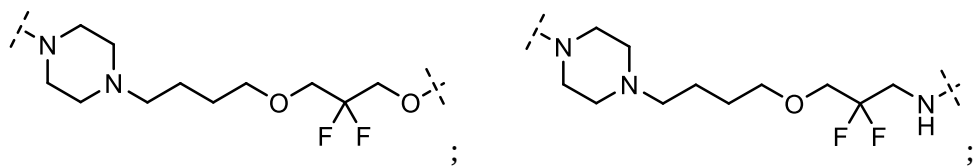
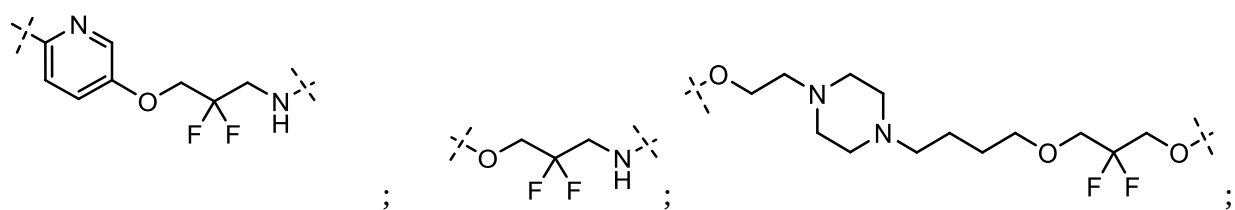


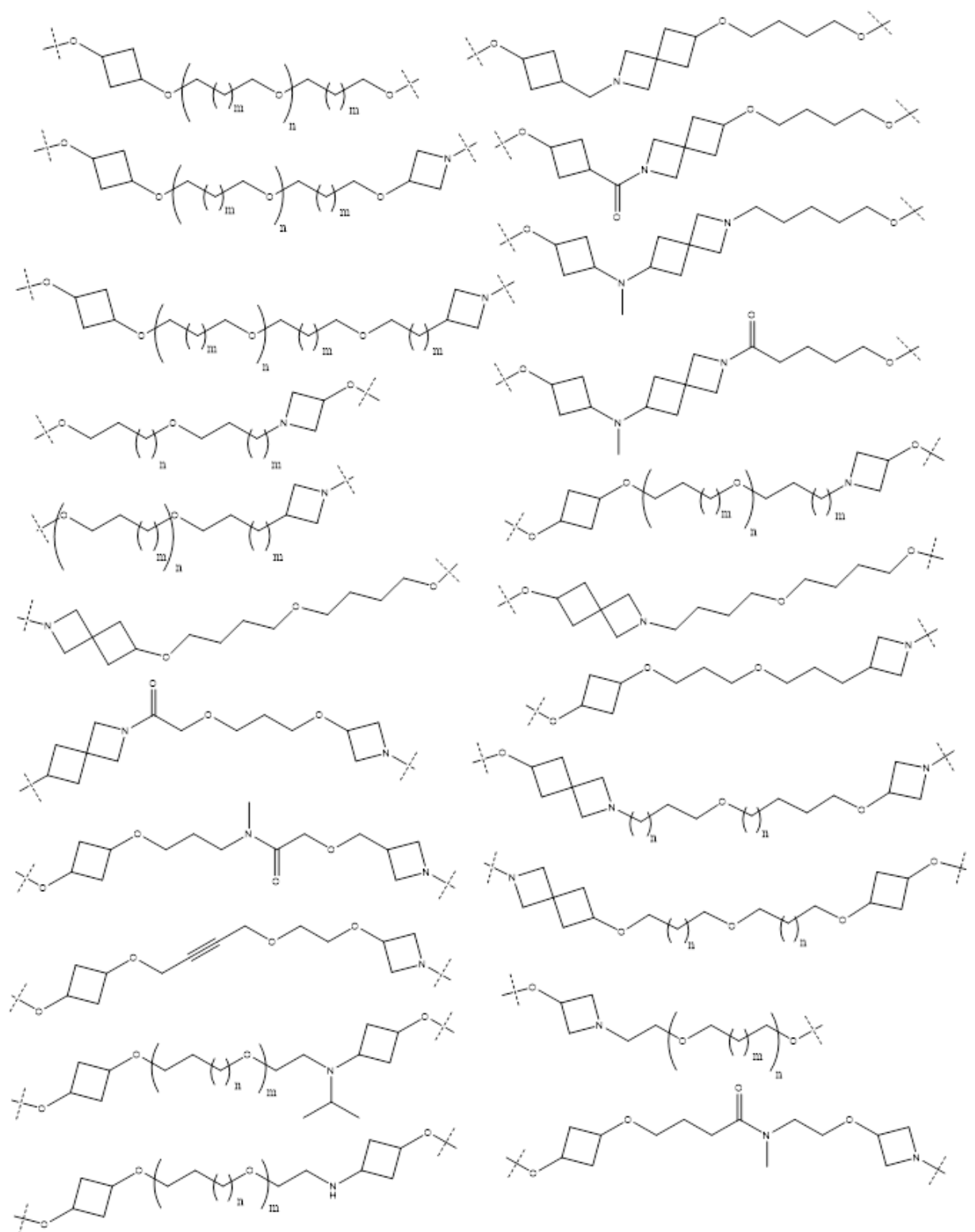


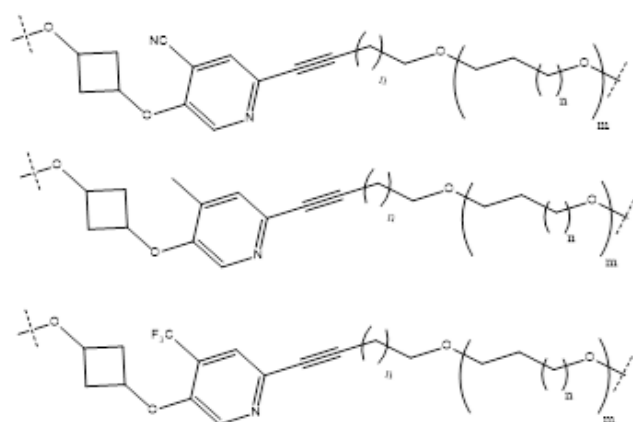
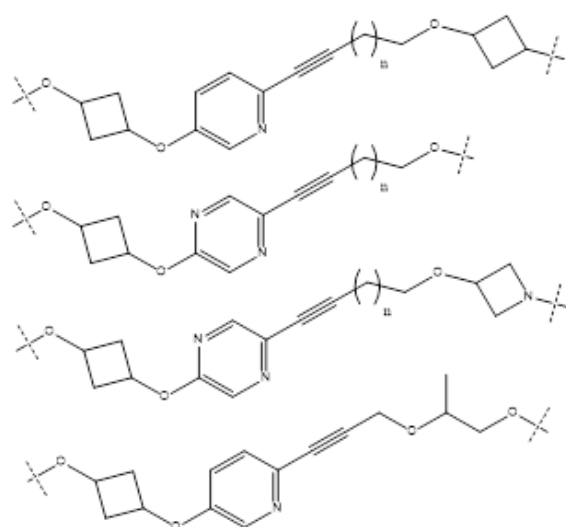
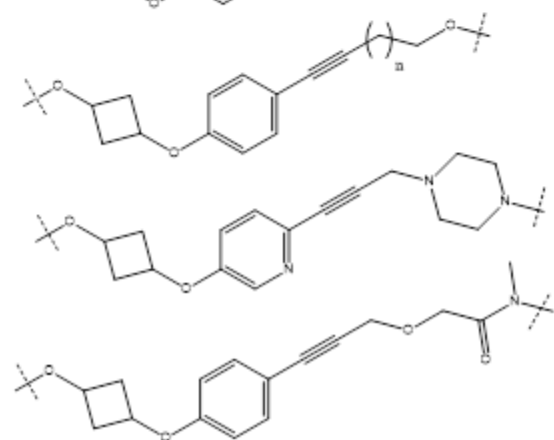
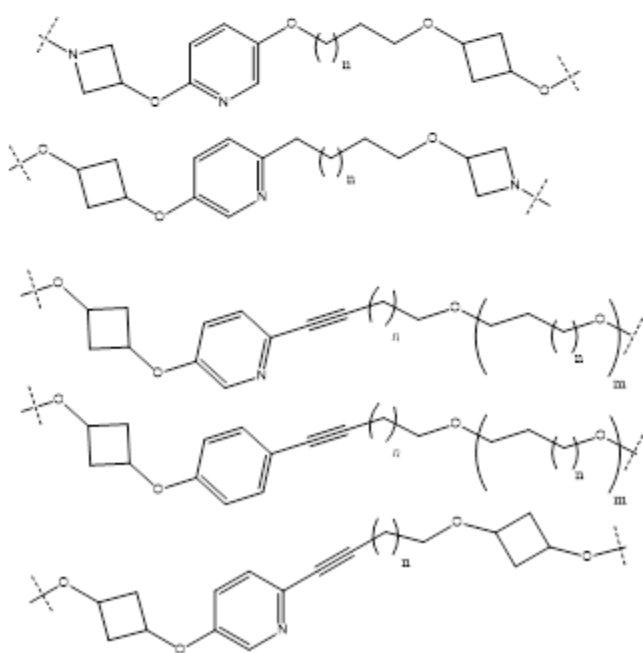
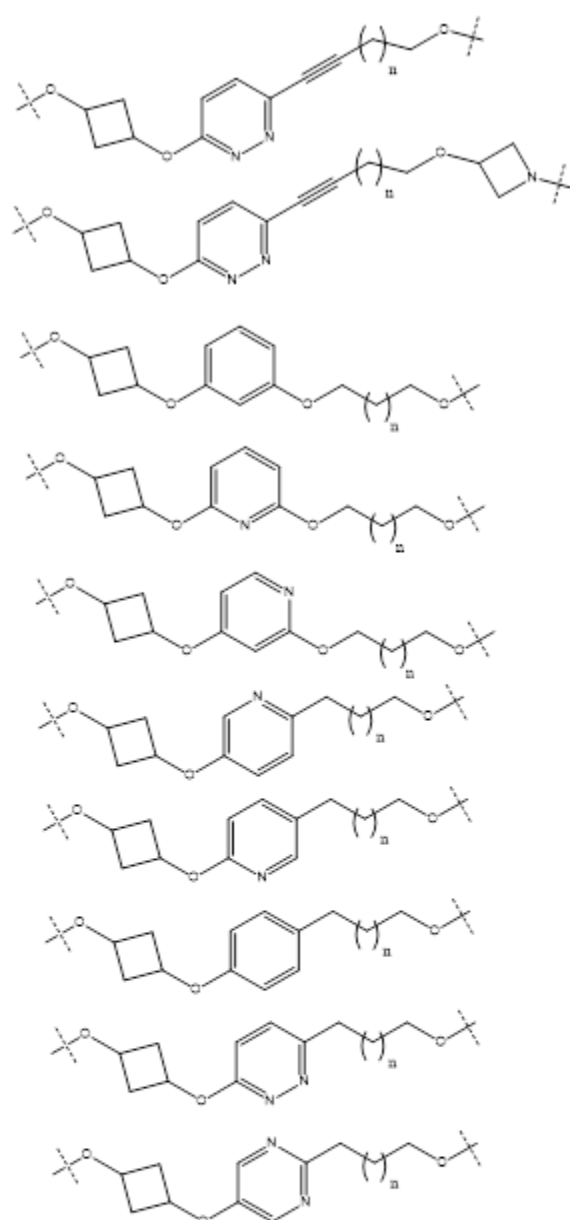
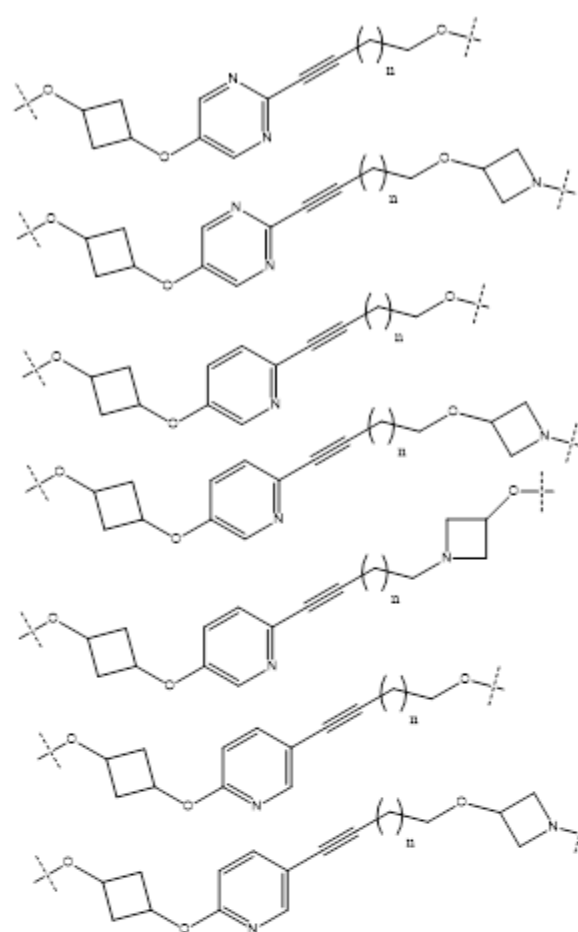
**238.** El compuesto de conformidad con cualquiera de las reivindicaciones 1-~~20~~a 5, en donde el enlazador (L) se selecciona del grupo que consiste en:

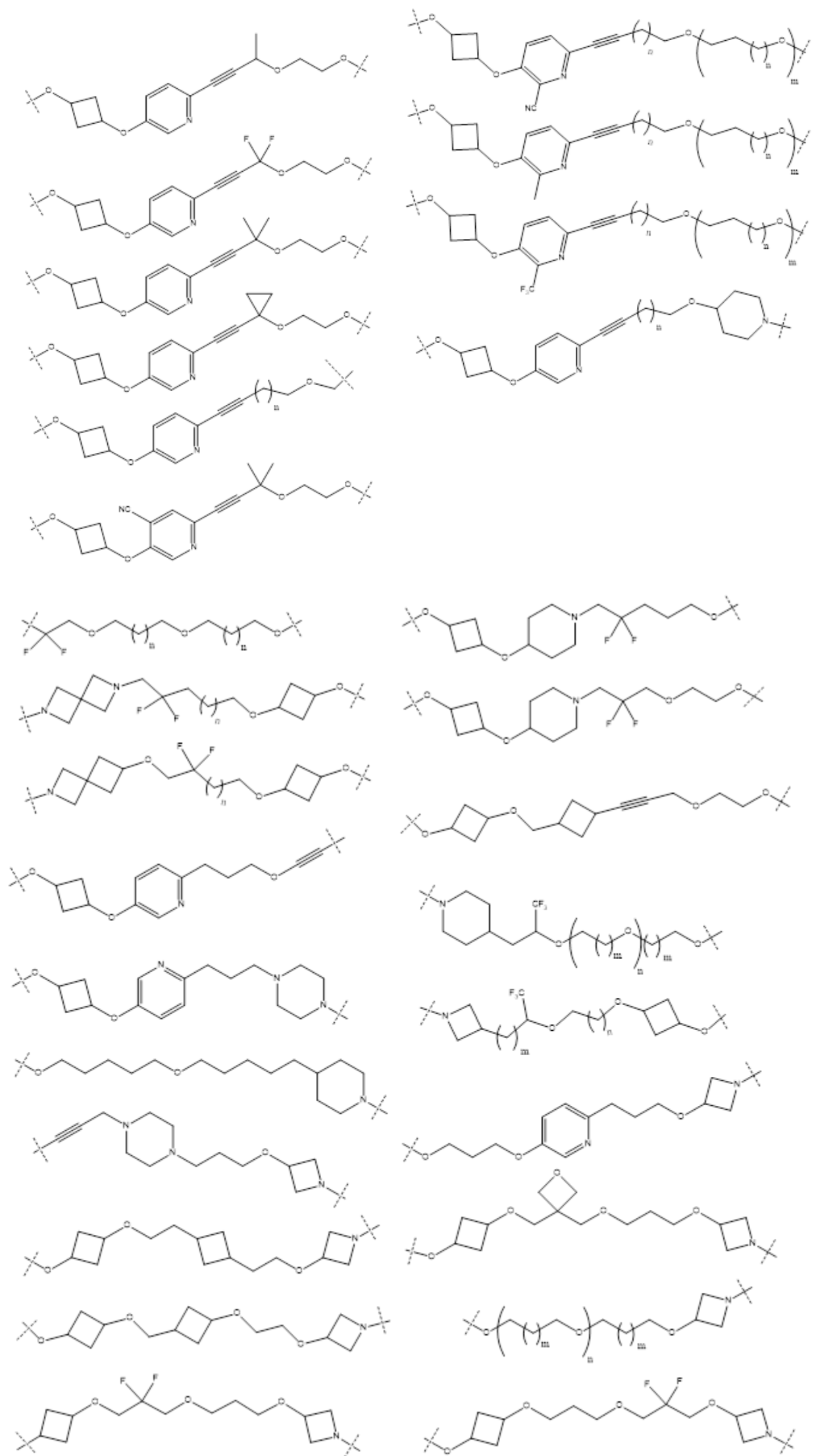


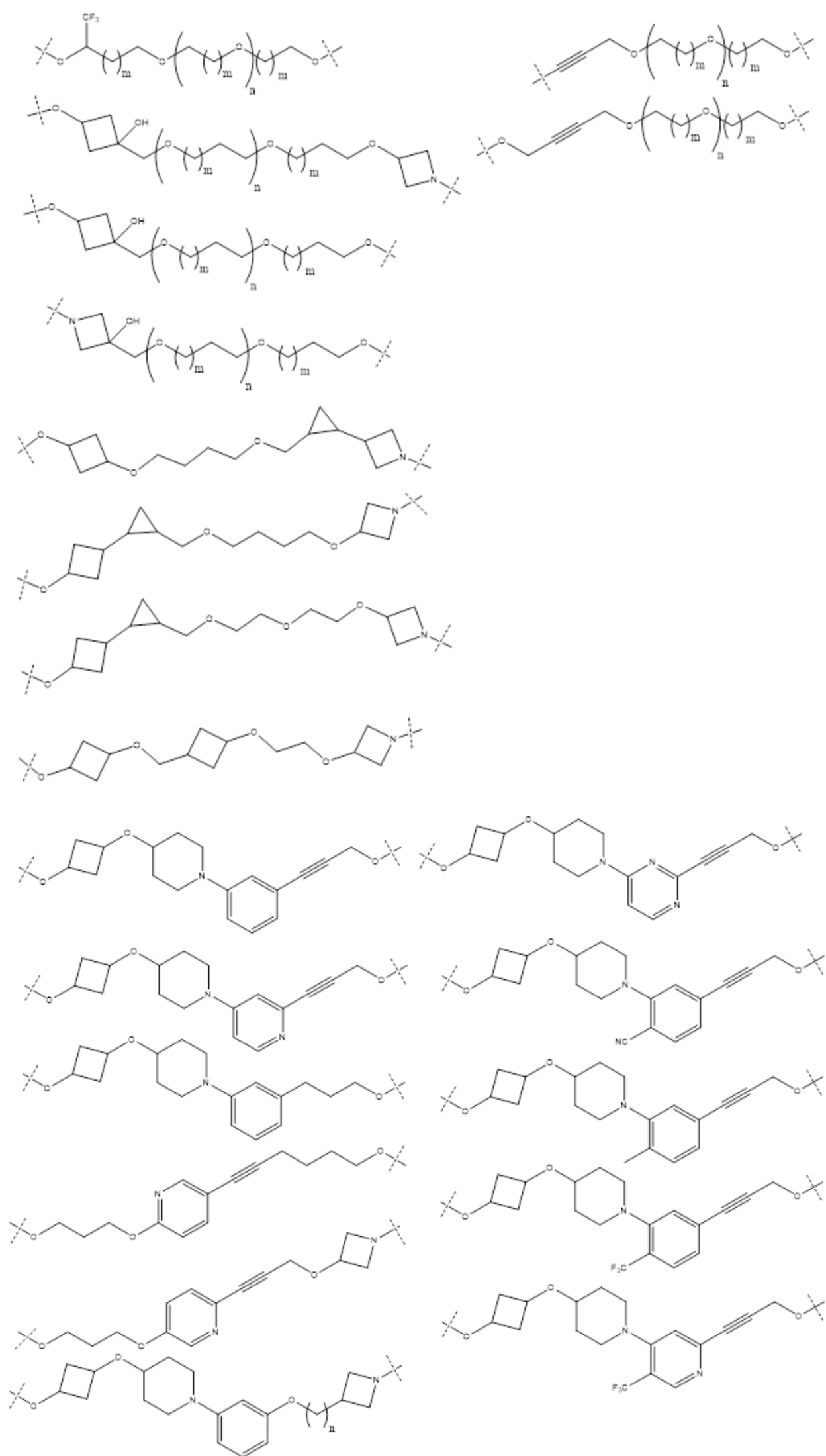


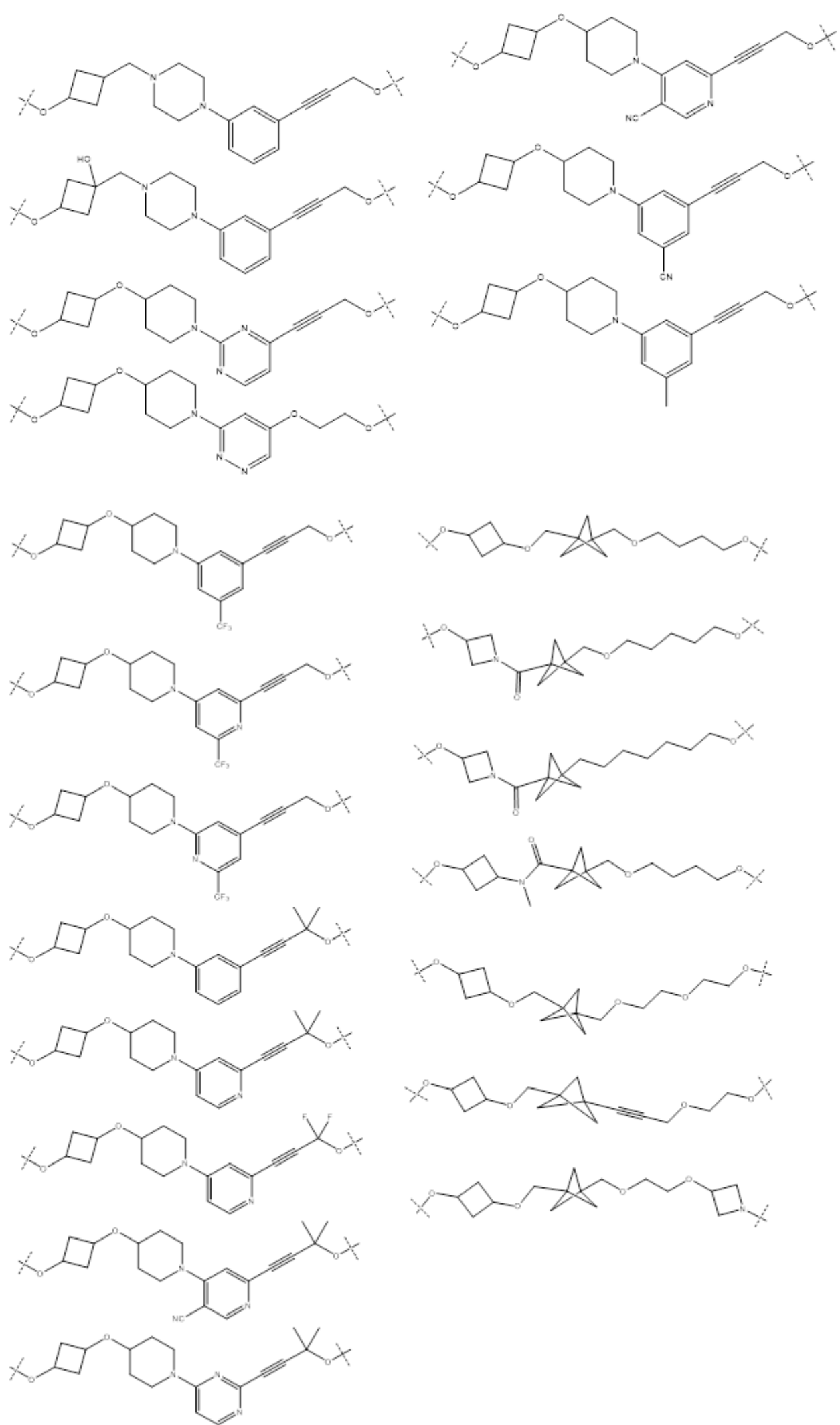


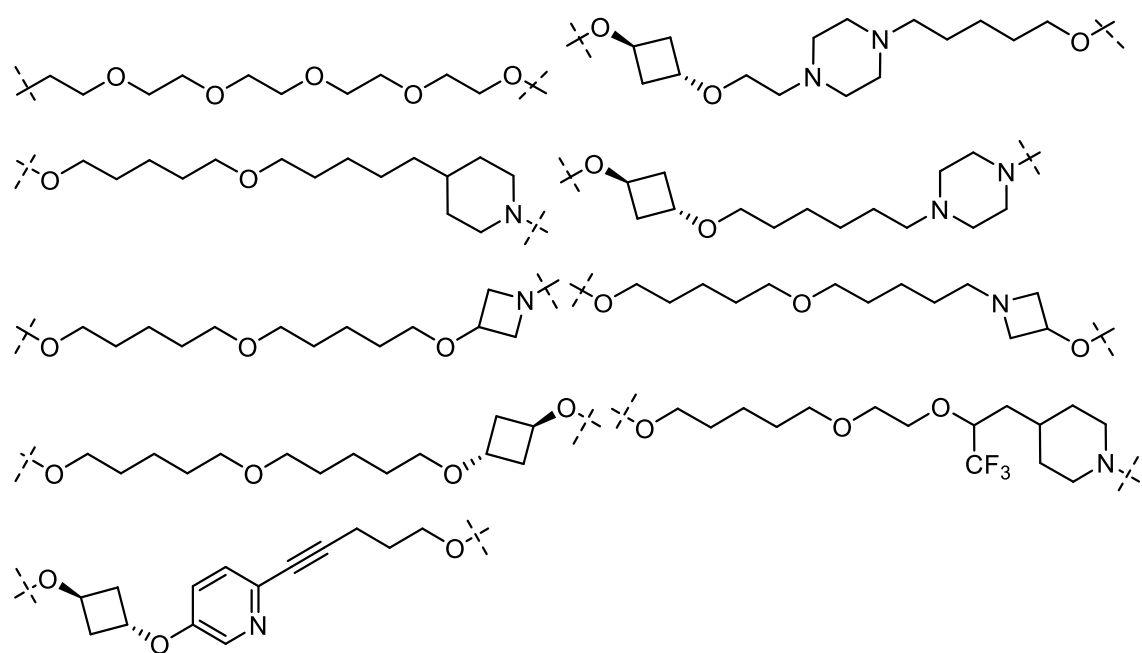
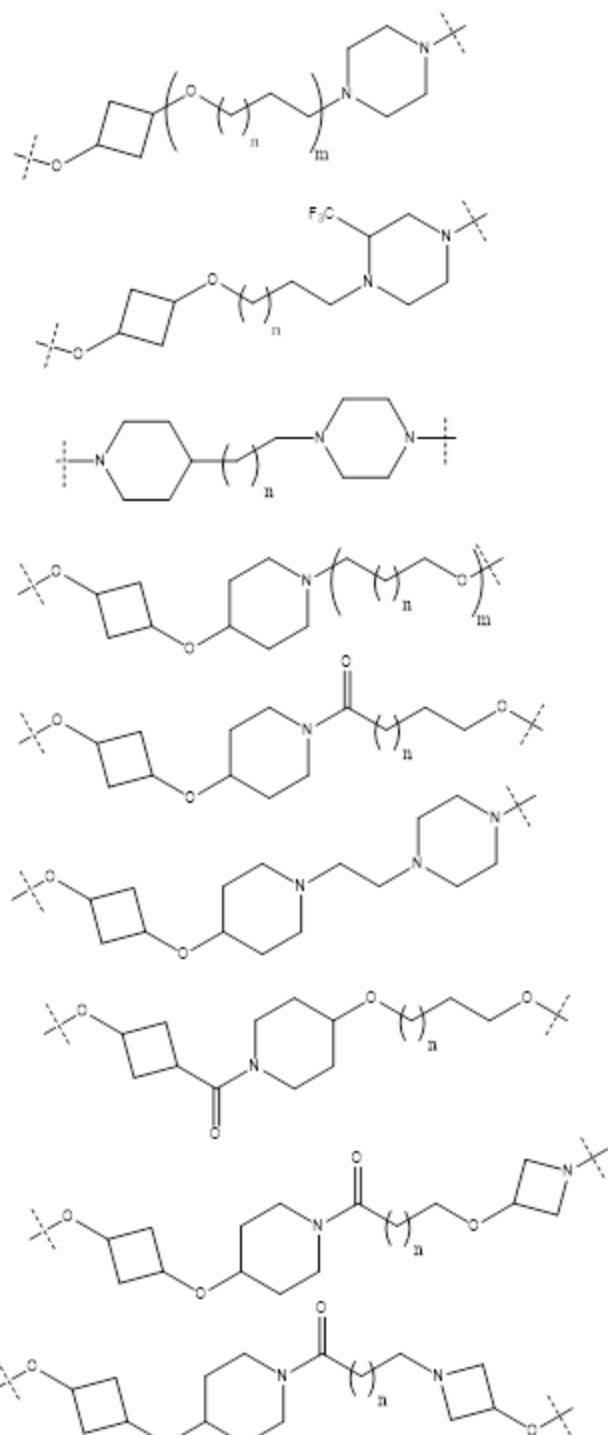






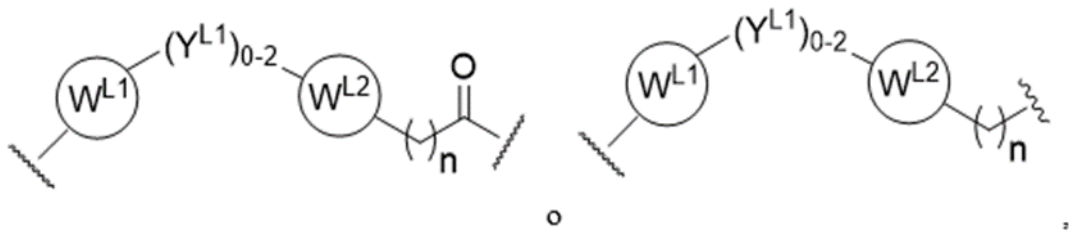






en donde cada n y m es independientemente 0, 1, 2, 3, 4, 5, o 6.

249. El compuesto de conformidad con cualquiera de las reivindicaciones 1-20 a 5, en donde el L comprende la siguiente estructura química:



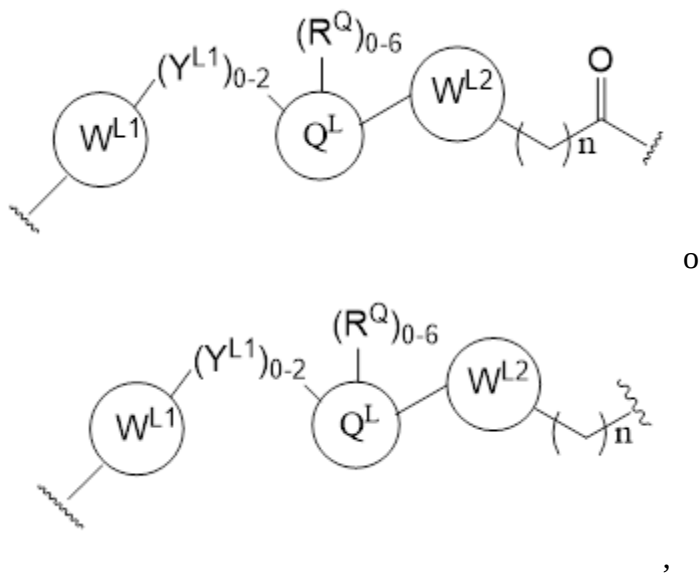
en donde:

$W^{L1}$  y  $W^{L2}$  son cada uno independientemente un anillo de 4-8 miembros con 0-4 heteroátomos, opcionalmente sustituidos con  $R^Q$ , cada  $R^Q$  es independientemente un H, halo, OH, CN,  $CF_3$ , alquilo de C1-C6 (lineal, o ramificado, ~~opcionalmente sustituido~~), alcoxi de C1-C6 (lineal, o ramificado, ~~opcionalmente sustituido~~), o 2 grupos  $R^Q$  tomados juntos con el átomo al que se unen para formar un sistema de anillos de 4-8 miembros que contiene 0-4 heteroátomos;

$Y^{L1}$  es cada uno independientemente un enlace, alquilo de C1-C6 (~~lineal, o ramificado, opcionalmente sustituido~~) con 1-3 halógenos y opcionalmente uno o más átomos de C se reemplazan con O; o alcoxi de C1-C6 (~~lineal, o ramificado, opcionalmente sustituido~~) con 1-3 halógenos; y

una línea discontinua indica el punto de acoplamiento a las porciones PTM o ULM.

2510. El compuesto de conformidad con las reivindicaciones 1-20 a 5, en donde L comprende la siguiente estructura química:



en donde:

$W^{L1}$  y  $W^{L2}$  son cada uno independientemente arilo de C<sub>6-10</sub>, heteroarilo de 6-10 miembros, cicloalquilo~~o~~ cíclico de 3-11 miembros, heterocíclico de 3-10 miembros, o alquilo de C<sub>1-6</sub>; ~~bicíclico, biarilo, biheteroarilo, o biheterocíclico~~, cada uno opcionalmente sustituido con  $R^Q$ , cada  $R^Q$  es independientemente un H, halo, OH, CN,  $CF_3$ , hidroxilo, nitro,  $C\equiv CH$ , alquenilo de C<sub>2-6</sub>, alquinilo de C<sub>2-6</sub>, alquilo de C<sub>1-6</sub> (~~lineal, o ramificado, opcionalmente~~

~~sustituído~~), alcoxi de C<sub>1</sub>-C<sub>6</sub> (lineal; o ramificado; ~~opcionalmente sustituido~~), OC<sub>1-3</sub>alquilo (opcionalmente sustituido por 1 o más –F), OH, NH<sub>2</sub>, NR<sup>Y1</sup>R<sup>Y2</sup>, CN, o 2 grupos R<sup>Q</sup> tomados juntos con el átomo al que se unen para formar un sistema de anillos de 4-8 miembros que contiene 0-4 heteroátomos;

Y<sup>YL1</sup> es cada uno independientemente un enlace, NR<sup>YL1</sup>, O, S, NR<sup>YL2</sup>, CR<sup>YL1</sup>R<sup>YL2</sup>, C=O, C=S, SO, SO<sub>2</sub>, C<sub>1</sub>-C<sub>6</sub> alquilo (lineal; o ramificado; ~~opcionalmente sustituido~~) y opcionalmente uno o más átomos de C se reemplazan con O; C<sub>1</sub>-C<sub>6</sub> alcoxi (lineal, ramificado, opcionalmente sustituido);

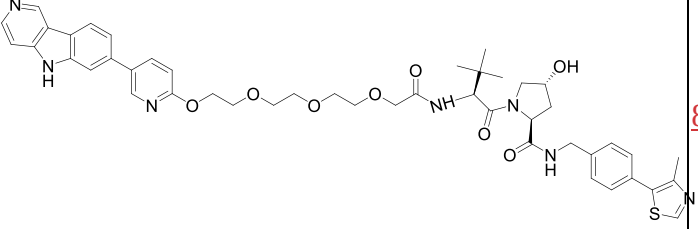
Q<sup>L</sup> es un anillo alicíclico o aromático de 3-6 miembros con 0-4 heteroátomos, que opcionalmente establecen puentes, opcionalmente sustituido con 0-6 R<sup>Q</sup>, cada R<sup>Q</sup> es independientemente H, o alquilo de C<sub>1-6</sub> (~~lineal; o ramificado~~, opcionalmente sustituido por 1 o más halo; o alcoxi de C<sub>1-6</sub>), o 2 grupos R<sup>Q</sup> tomados juntos con el átomo al que se unen para formar un sistema de anillos de 3-8 miembros que contiene 0-2 heteroátomos);

R<sup>YL1</sup>, R<sup>YL2</sup> son cada uno independientemente H, OH, alquilo de C<sub>1-6</sub> (~~lineal; o ramificado~~, opcionalmente sustituido por 1 o más halo; o alcóxido de C<sub>1-6</sub>), o R<sup>1</sup>, R<sup>2</sup> junto con el átomo al que se unen para formar un sistema de anillos de 3-8 miembros que contiene 0-2 heteroátomos);

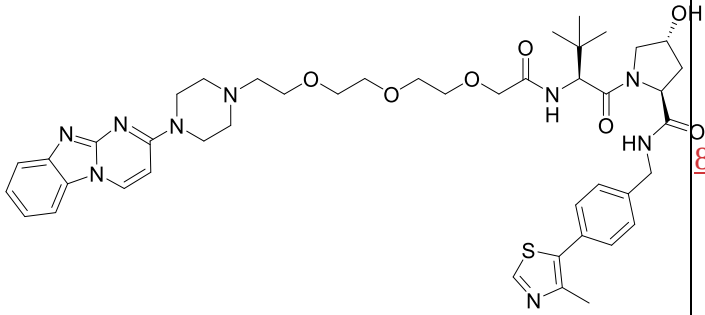
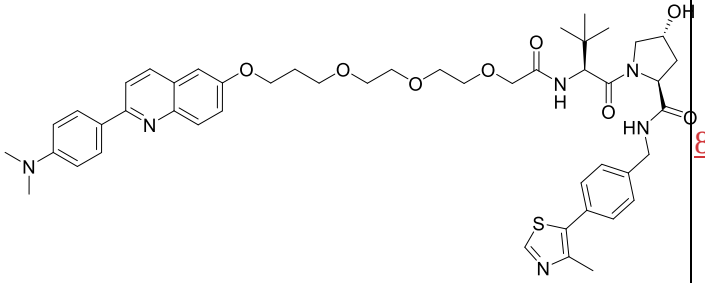
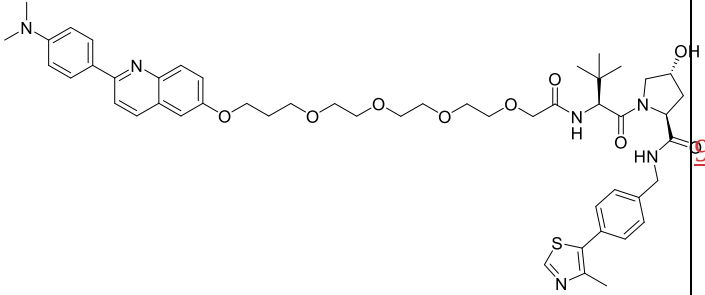
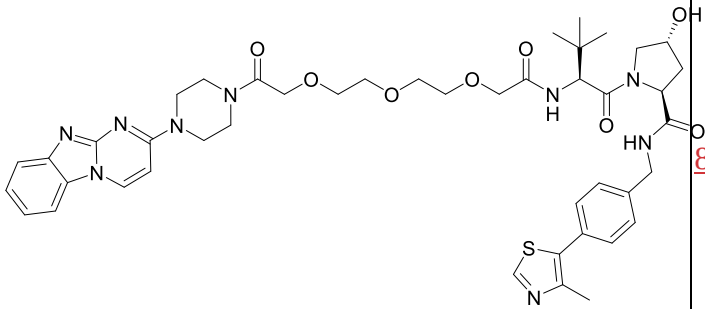
n es 0-10; y  
una línea discontinua indica el punto de acoplamiento a las porciones PTM o ULM.

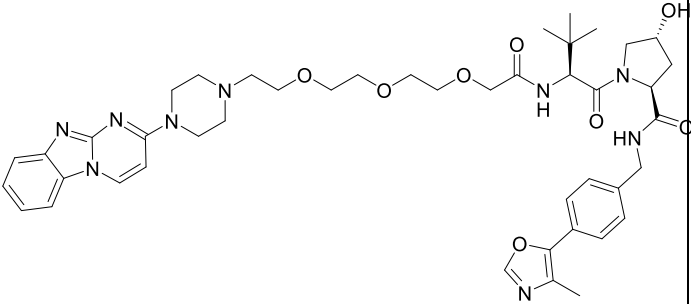
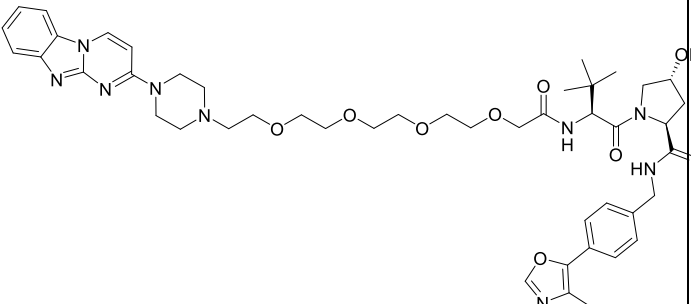
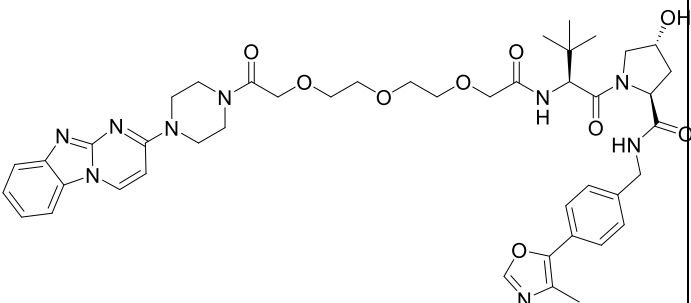
**2611.** El compuesto de conformidad con cualquiera de las reivindicaciones 1-~~20~~ a 5, en donde el L es un grupo polietilenoxi opcionalmente sustituido con arilo de C<sub>6-10</sub> ~~o fenilo~~ que comprende de 1 a 10 unidades de etilenglicol.

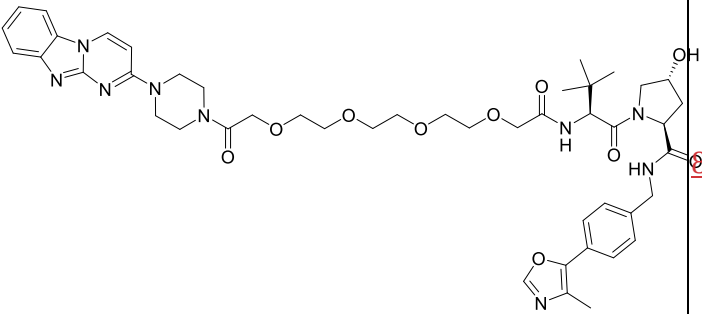
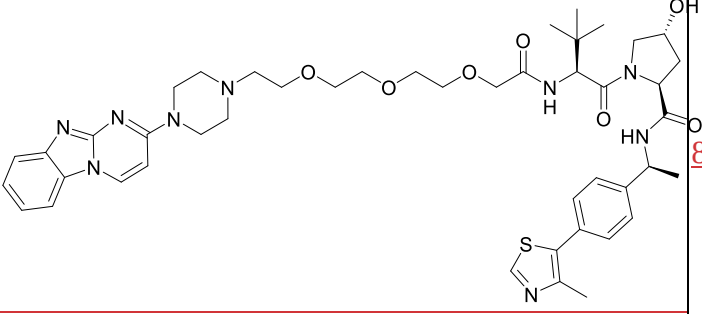
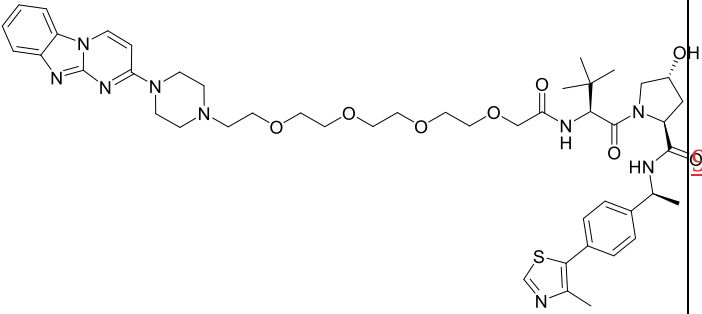
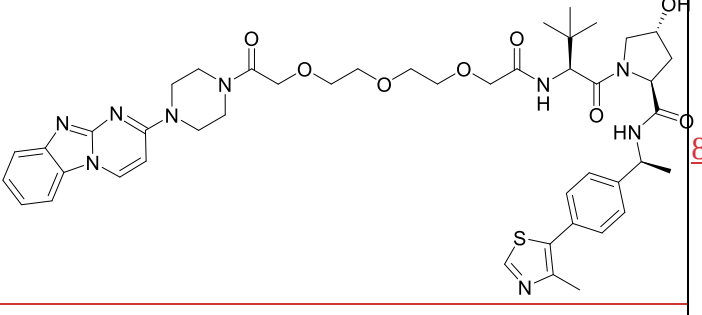
**2712.** El compuesto bifuncional de cualquiera de las reivindicaciones 1-~~26~~ a 11, en donde el compuesto se selecciona del grupo que consiste en los siguientes ~~compuestos 1-330~~ (Tabla 1 y Tabla 2):

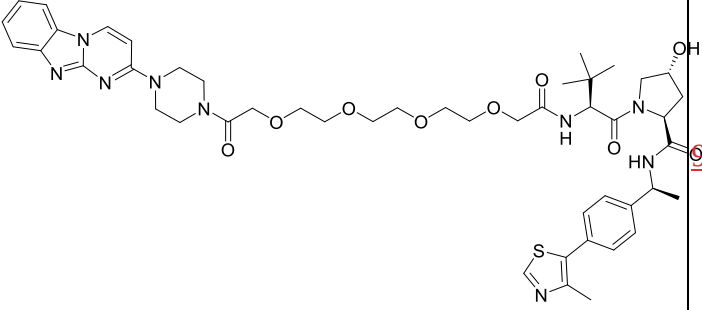
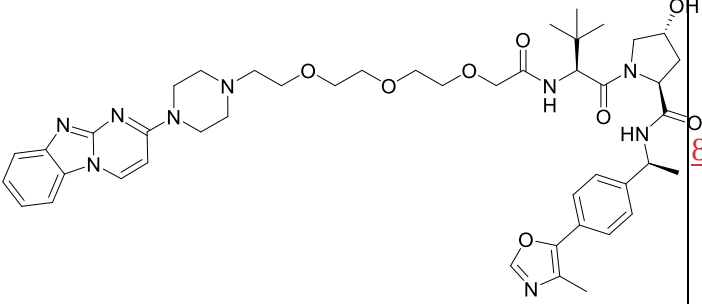
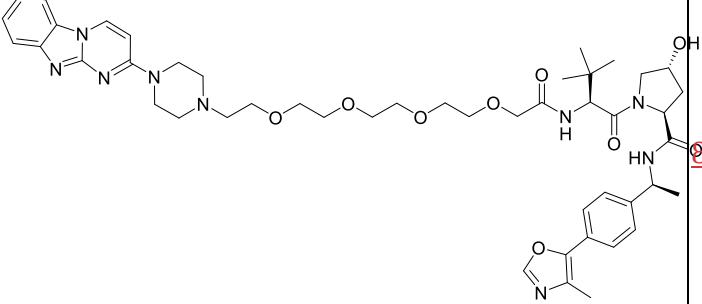
| #        | Estructura                                                                          | (M+H) <sup>+</sup> | Datos de NMR                                                                                                                                                                                                                                                                                                                                                                                                                                 | Actividad* |
|----------|-------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| <u>1</u> |  | <u>864.3</u>       | <u><sup>1</sup>HNMR (400 MHz, MeOD) : δ 9.39 (s, 1H), 8.82 (s, 1H), 8.47-8.45 (m, 2H), 8.33 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 6.4 Hz, 1H), 7.81 (s, 1H), 7.73 (d, J = 6.0 Hz, 1H), 7.63 (d, J = 6.0 Hz, 1H), 7.43-7.36 (m, 4H), 6.92 (d, J = 8.4 Hz, 1H), 4.78 (s, 1H), 4.69-4.50 (m, 5H), 4.43-4.31 (m, 1H), 4.04-4.02 (m, 2H), 3.87-3.85 (m, 3H), 3.73-3.64 (m, 9H), 2.40 (s, 3H), 2.25-2.19 (m, 1H), 2.15-2.10 (m, 1H), 1.03 (s, 9H).</u> |            |

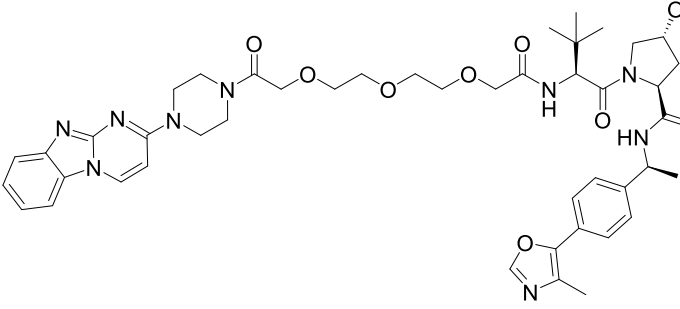
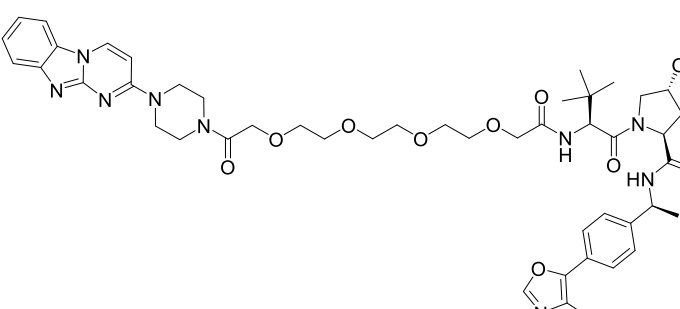
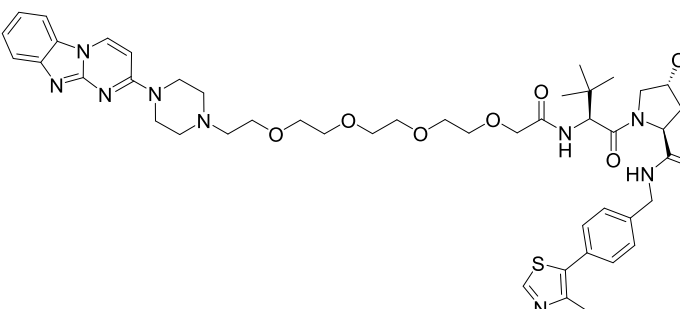
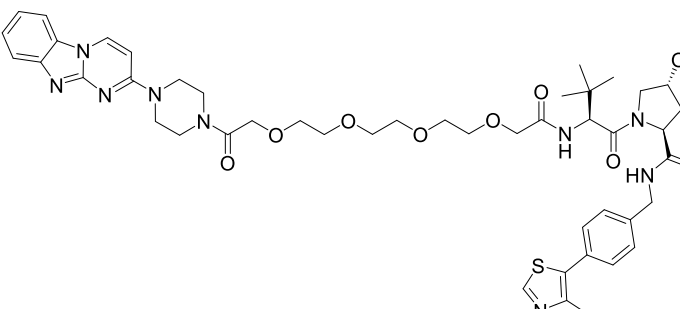


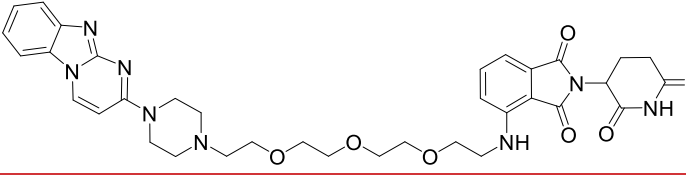
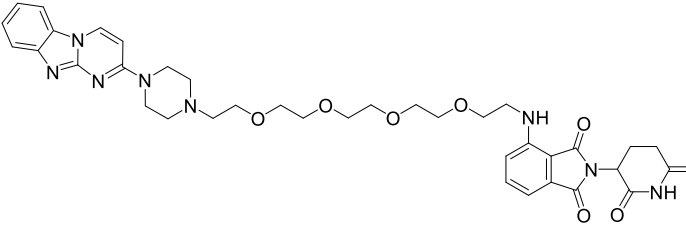
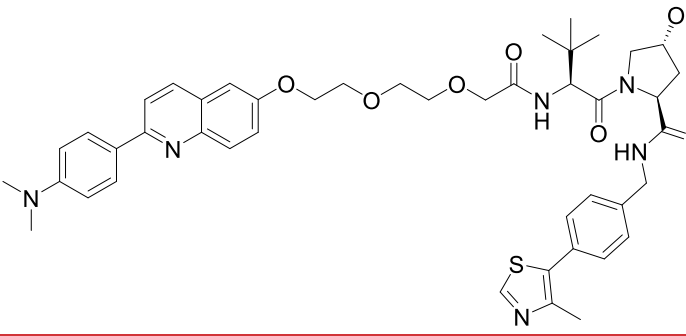
|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |
|----|-------------------------------------------------------------------------------------|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
| 7  |    | 856.5 | <sup>1</sup> H NMR (400MHz, MeOD): δ 8.85 (s, 1H), 8.71 (d, <i>J</i> = 7.6 Hz, 1H), 7.70 (d, <i>J</i> = 8.0 Hz, 1H), 7.55 (d, <i>J</i> = 8.0 Hz, 1H), 7.34-7.42 (m, 5H), 7.22-7.23 (m, 1H), 6.76 (d, <i>J</i> = 7.6 Hz, 1H), 4.68 (s, 1H), 4.47-4.57 (m, 4H), 4.30-4.39 (m, 1H), 4.05 (s, 3H), 3.56-4.87 (m, 23H), 2.64(s, 4H), 2.45 (s, 3H), 2.19 (br, 1H), 2.04 (br, 1H), 1.03 (s, 9H).                                                           | C |
| 8  |   | 881.6 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.02 (s, 9H), 2.07-2.25 (m, 4H), 2.46 (s, 3H), 3.04 (s, 6H), 3.65-3.71 (m, 10H), 3.78-3.86 (m, 2H), 4.01-4.06 (m, 2H), 4.18-4.21 (m, 2H), 4.32-4.36 (m, 1H), 4.50-4.60 (m, 3H), 4.68-4.70 (m, 1H), 6.88 (d, <i>J</i> = 9.2 Hz, 2H), 7.23-7.26 (m, 1H), 7.34-7.44 (m, 5H), 7.82 (d, <i>J</i> = 8.4 Hz, 1H), 7.92-7.96 (m, 3H), 8.16 (d, <i>J</i> = 8.8 Hz, 1H), 8.86 (s, 1H).                     | C |
| 9  |  | 925.6 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.04 (s, 9H), 2.08-2.12 (m, 3H), 2.20-2.23 (m, 1H), 2.46 (s, 3H), 3.04 (s, 6H), 3.62-3.71 (m, 14H), 3.78-3.89 (m, 2H), 4.01-4.19 (m, 2H), 4.14-4.23 (m, 2H), 4.33-4.37 (m, 1H), 4.51-4.58 (m, 3H), 4.68-4.70 (m, 1H), 6.68 (d, <i>J</i> = 8.4 Hz, 1H), 7.24 (br, 1H), 7.36-7.45 (m, 5H), 7.62-7.64 (m, 1H), 7.79-7.84 (m, 1H), 7.93-7.97 (m, 3H), 8.17 (d, <i>J</i> = 8.0 Hz, 1H), 8.68 (s, 1H). | C |
| 10 |  | 870.5 | <sup>1</sup> H NMR (400MHz, MeOD): δ 8.85 (s, 1H), 8.77 (d, <i>J</i> = 8.0 Hz, 1H), 7.83 (d, <i>J</i> = 8.0 Hz, 1H), 7.57 (d, <i>J</i> = 8.0 Hz, 1H), 7.37-7.45 (m, 5H), 7.25 (t, <i>J</i> = 8.0 Hz, 1H), 6.79 (d, <i>J</i> = 8.0 Hz, 1H), 4.68 (s, 1H), 4.49-4.60 (m, 3H), 4.24-4.36 (m, 3H), 4.01-4.06 (m, 2H), 3.91-3.98 (m, 2H), 3.86-3.89 (m, 2H), 3.65-3.80 (m, 14H), 2.45 (s, 3H), 2.20-                                                     | C |

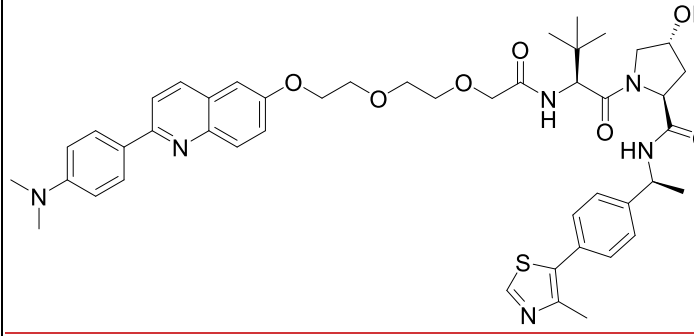
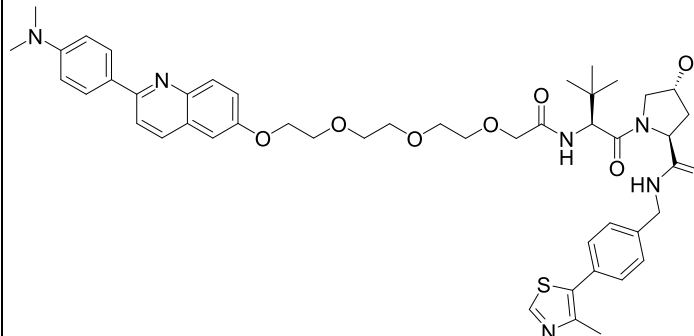
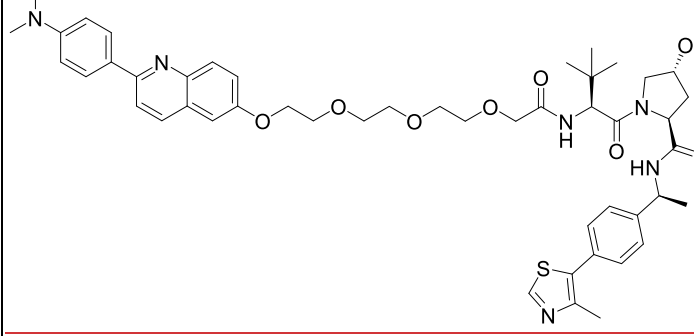
|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |
|----|-------------------------------------------------------------------------------------|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
|    |                                                                                     |       | <p>2.26 (m, 1H), 2.04–2.11 (m, 1H), 1.03 (s, 9H).</p>                                                                                                                                                                                                                                                                                                                                                                                                                                          |   |
| 11 |   | 840.6 | <p><sup>1</sup>H NMR (400 MHz, MeOD): δ 8.70 (d, <i>J</i> = 7.6 Hz, 1H), 8.11 (s, 1H), 7.80 (d, <i>J</i> = 8.4 Hz, 1H), 7.53–7.55 (m, 3H), 7.43 (d, <i>J</i> = 8.4 Hz, 2H), 7.37 (t, <i>J</i> = 8.0 Hz, 2H), 7.23 (d, <i>J</i> = 7.6 Hz, 1H), 6.76 (d, <i>J</i> = 7.6 Hz, 1H), 4.84 (s, 1H), 4.53–4.60 (m, 1H), 4.49 (s, 1H), 4.31–4.35 (m, 1H), 4.05 (s, 2H), 3.77–3.80 (m, 5H), 3.65–3.70 (m, 10H), 2.64–2.66 (m, 6H), 2.36 (s, 3H), 2.11–2.20 (m, 1H), 2.04–2.10 (m, 1H), 1.04 (s, 9H).</p> | C |
| 12 |  | 884.4 | <p><sup>1</sup>H NMR (400 MHz, MeOD): δ 8.71 (br, 1H), 8.12 (s, 1H), 7.80–7.82 (m, 1H), 7.43–7.56 (m, 3H), 7.35–7.39 (m, 3H), 7.24–7.25 (m, 1H), 6.76–6.78 (m, 1H), 4.49 (s, 1H), 4.54–4.58 (m, 3H), 4.32–4.36 (m, 1H), 4.04 (s, 1H), 3.81–3.92 (m, 5H), 3.61–3.69 (m, 12H), 3.35 (s, 1H), 2.66–2.75 (m, 6H), 2.37 (s, 3H), 2.20–2.22 (m, 1H), 2.07–2.15 (m, 1H), 1.04 (s, 9H).</p>                                                                                                            | C |
| 13 |  | 854.5 | <p><sup>1</sup>H NMR (400 MHz, MeOD): δ 8.79 (d, <i>J</i> = 7.6 Hz, 1H), 8.12 (s, 1H), 7.85 (d, <i>J</i> = 8.0 Hz, 1H), 7.54–7.58 (m, 3H), 7.39–7.43 (m, 2H), 7.28 (t, <i>J</i> = 7.6 Hz, 1H), 6.83 (d, <i>J</i> = 8.0 Hz, 1H), 4.68 (s, 1H), 4.67 (s, 1H), 4.55–4.61 (m, 1H), 4.44 (br, 1H), 4.29–4.35 (m, 5H), 3.80–4.03 (m, 8H), 3.71–3.82 (m, 13H), 3.37 (s, 3H), 2.20–2.22 (s, 1H), 2.08–2.10 (m, 1H), 1.04 (s, 9H).</p>                                                                  | C |

|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |   |
|----|-------------------------------------------------------------------------------------|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
| 14 |    | 898.6 | <sup>1</sup> H NMR (400 MHz, MeOD): $\delta$ 8.76 (d, $J$ = 7.2 Hz, 1H), 8.09 (s, 1H), 7.84 (d, $J$ = 7.2 Hz, 1H), 7.35–7.63 (m, 6H), 7.28 (t, $J$ = 7.6 Hz, 1H), 6.82 (d, $J$ = 7.6 Hz, 1H), 4.68 (s, 1H), 4.50–4.61 (m, 3H), 4.28–4.39 (m, 3H), 4.06 (s, 2H), 3.86–3.97 (m, 3H), 3.78–3.81 (m, 1H), 3.55–3.76 (m, 16H), 3.18–3.23 (m, 2H), 2.35 (s, 3H), 2.21–2.26 (m, 1H), 2.04–2.10 (m, 1H), 1.04 (s, 9H).                                                         | C |
| 15 |   | 870.6 | <sup>1</sup> H NMR (400 MHz, MeOD): $\delta$ 8.85 (s, 1H), 8.76 (d, $J$ = 8.0 Hz, 1H), 7.83 (d, $J$ = 8.0 Hz, 1H), 7.56 (d, $J$ = 7.6 Hz, 1H), 7.37–7.40 (m, 6H), 7.26 (t, $J$ = 7.2 Hz, 1H), 6.84 (d, $J$ = 8.0 Hz, 1H), 4.99–5.01 (m, 1H), 4.68 (s, 1H), 4.57 (t, $J$ = 7.6 Hz, 1H), 4.44 (s, 1H), 4.05 (br, 2H), 3.83–3.91 (m, 5H), 3.68–3.76 (m, 12H), 2.70 (m, 6H), 2.45 (s, 3H), 2.17–2.20 (m, 1H), 1.96–2.05 (m, 1H), 1.56 (d, $J$ = 7.2 Hz, 3H), 1.05 (s, 9H). | C |
| 16 |  | 914.6 | <sup>1</sup> H NMR (400 MHz, MeOD): $\delta$ 8.80–8.85 (m, 2H), 7.88 (d, $J$ = 8.0 Hz, 1H), 7.57 (d, $J$ = 8.0 Hz, 1H), 7.32–7.46 (m, 7H), 6.93 (d, $J$ = 8.0 Hz, 1H), 4.99–5.01 (m, 1H), 4.68 (s, 1H), 4.55–4.57 (m, 1H), 4.43 (s, 1H), 4.04 (s, 2H), 3.80–3.94 (m, 4H), 3.83–3.85 (m, 15H), 2.72–2.74 (m, 6H), 2.46 (s, 3H), 2.12–2.13 (m, 1H), 1.97–1.99 (m, 1H), 1.96–2.05 (m, 1H), 1.56 (d, $J$ = 7.2 Hz, 3H), 1.05 (s, 9H).                                      | C |
| 17 |  | 884.5 | <sup>1</sup> H NMR (400 MHz, MeOD): $\delta$ 8.85 (s, 1H), 8.78 (d, $J$ = 7.6 Hz, 1H), 7.83 (d, $J$ = 7.6 Hz, 1H), 7.57 (d, $J$ = 7.6 Hz, 1H), 7.35–7.40 (m, 6H), 7.23 (t, $J$ = 8.0 Hz, 1H), 4.98–5.00 (m, 1H), 4.67 (s, 1H), 4.55–4.57 (m, 1H), 4.34–4.43 (m, 3H), 3.83–4.03 (m, 7H), 3.72–3.74                                                                                                                                                                      | C |

|           |                                                                                     |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |          |
|-----------|-------------------------------------------------------------------------------------|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|
|           |                                                                                     |              | (m, 16H), 2.46 (s, 3H),<br>2.17–2.21 (m, 1H), 1.95–<br>2.10 (m, 1H), 1.31 (d, <i>J</i> =<br>8.8 Hz, 3H), 1.03 (s, 9H).                                                                                                                                                                                                                                                                                                                                                                                                                                                  |          |
| <u>18</u> |    | <u>928.7</u> | <sup>1</sup> H NMR (400 MHz,<br>MeOD): δ 8.75–8.86 (m,<br>2H), 7.85 (d, <i>J</i> = 8.0 Hz,<br>1H), 7.56 (d, <i>J</i> = 8.0 Hz,<br>1H), 7.34–7.42 (m, 5H),<br>7.27 (t, <i>J</i> = 7.6 Hz, 1H),<br>6.79–6.85 (m, 1H), 4.94–<br>5.04 (m, 1H), 4.67 (s,<br>1H), 4.55–4.61 (m, 1H),<br>4.44 (br, 1H), 4.29–4.35<br>(m, 2H), 4.07 (s, 2H),<br>3.83–3.96 (m, 4H), 3.61–<br>3.79 (m, 16H), 3.18–3.23<br>(m, 2H), 2.45 (s, 3H),<br>2.18–2.23 (m, 1H), 1.92–<br>1.99 (m, 1H), 1.48–1.57<br>(m, 3H), 1.03 (s, 9H).                                                                 | <u>C</u> |
| <u>19</u> |  | <u>854.6</u> | <sup>1</sup> H NMR (400 MHz,<br>MeOD): δ 8.76 (d, <i>J</i> =<br>7.6 Hz, 1H), 8.11 (s, 1H),<br>7.84 (d, <i>J</i> = 8.0 Hz, 1H),<br>7.56 (t, <i>J</i> = 8.4 Hz, 3H),<br>7.40 (d, <i>J</i> = 8.4 Hz, 3H),<br>7.27 (t, <i>J</i> = 8.0 Hz, 1H),<br>6.85 (m, <i>J</i> = 7.6 Hz, 1H),<br>4.98–4.50 (m, 1H), 4.75<br>(s, 1H), 4.57 (t, <i>J</i> = 7.6<br>Hz, 1H), 4.43 (s, 1H),<br>4.05 (s, 2H), 3.83–3.91<br>(m, 5H), 3.67–3.76 (m,<br>12H), 2.70–2.71 (m, 6H),<br>2.37 (s, 3H), 2.17–2.19<br>(m, 1H), 1.95–2.10 (m,<br>1H), 1.55 (d, <i>J</i> = 6.4 Hz,<br>3H), 1.05 (s, 9H). | <u>C</u> |
| <u>20</u> |  | <u>998.6</u> | <sup>1</sup> H NMR (400 MHz,<br>MeOD): δ 8.72 (d, <i>J</i> =<br>8.0 Hz, 1H), 8.11 (s, 1H),<br>7.81 (d, <i>J</i> = 8.0 Hz, 1H),<br>7.54–7.56 (m, 3H),<br>7.35–7.41 (m, 3H), 7.24<br>(t, <i>J</i> = 8.0 Hz, 1H), 6.79<br>(d, <i>J</i> = 8.0 Hz, 1H), 4.96–<br>4.50 (m, 1H), 4.68 (s,<br>1H), 4.55–4.59 (m, 1H),<br>4.43 (s, 1H), 4.04 (s, 2H),<br>3.74–3.89 (m, 5H), 3.68–<br>3.70 (m, 18H), 2.68–2.72<br>(m, 6H), 2.37 (s, 3H),<br>2.17–2.19 (m, 1H), 1.95–<br>2.10 (m, 1H), 1.50 (d, <i>J</i> =<br>6.4 Hz, 3H), 1.04 (s, 9H).                                           | <u>C</u> |

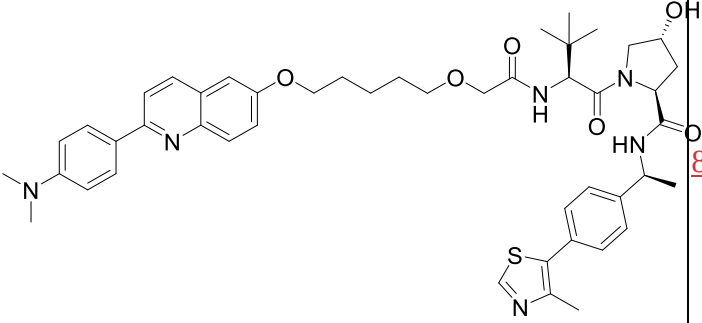
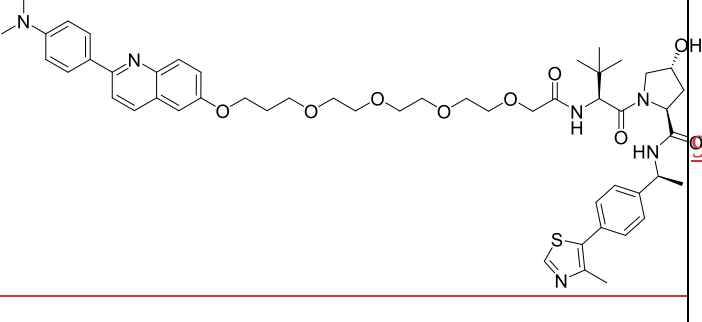
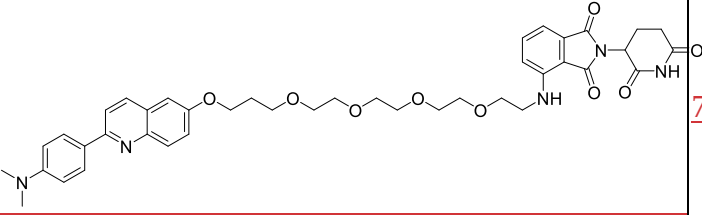
|                  |                                                                                     |                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|------------------|-------------------------------------------------------------------------------------|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p><u>21</u></p> |    | <p><u>868.3</u></p> | <p><sup>1</sup>H NMR (400 MHz, MeOD): <math>\delta</math> 8.77 (d, <math>J</math> = 8.0 Hz, 1H), 8.12 (s, 1H), 7.82 (d, <math>J</math> = 8.0 Hz, 1H), 7.56–7.58 (m, 3H), 7.35–7.41 (m, 3H), 7.23 (d, <math>J</math> = 8.0 Hz, 1H), 6.79 (d, <math>J</math> = 7.6 Hz, 1H), 4.98–4.99 (m, 1H), 4.67 (s, 1H), 4.55–4.59 (m, 1H), 4.43 (s, 1H), 4.33–4.35 (m, 2H), 3.86–4.01 (m, 7H), 3.72–3.74 (m, 14H), 2.38 (s, 3H), 2.17–2.19 (m, 1H), 1.95–2.05 (m, 1H), 1.48 (d, <math>J</math> = 6.8 Hz, 3H), 1.03 (s, 9H).</p> |
| <p><u>22</u></p> |   | <p><u>912.6</u></p> | <p><sup>1</sup>H NMR (400 MHz, MeOD): <math>\delta</math> 8.75–8.81 (m, 1H), 8.06–8.10 (m, 1H), 7.86 (d, <math>J</math> = 8.0 Hz, 1H), 7.55–7.61 (m, 3H), 7.35–7.43 (m, 3H), 7.25–7.31 (m, 1H), 6.81–6.88 (m, 1H), 4.94–5.04 (m, 1H), 4.67 (s, 1H), 4.55–4.60 (m, 1H), 4.43 (br, 1H), 4.35 (s, 2H), 4.07 (s, 2H), 3.91–3.97 (m, 3H), 3.82–3.85 (m, 1H), 3.61–3.79 (m, 16H), 3.18–3.23 (m, 2H), 2.37 (s, 3H), 2.18–2.23 (m, 1H), 1.92–1.99 (m, 1H), 1.48–1.56 (m, 3H), 1.04 (s, 9H).</p>                            |
| <p><u>23</u></p> |  | <p><u>900.6</u></p> | <p><sup>1</sup>H NMR (400 MHz, MeOD): <math>\delta</math> 8.85 (s, 1H), 8.70 (d, <math>J</math> = 8.0 Hz, 1H), 7.79 (d, <math>J</math> = 8.0 Hz, 1H), 7.54 (d, <math>J</math> = 8.0 Hz, 1H), 7.34–7.44 (m, 5H), 7.24 (t, <math>J</math> = 6.8 Hz, 4.8 Hz, 1H), 6.75 (d, <math>J</math> = 8.0 Hz, 1H), 4.69 (s, 1H), 4.57 (m, 3H), 4.50 (d, <math>J</math> = 4.8 Hz, 1H), 4.04 (s, 2H), 3.85 (s, 6H), 3.60–3.69 (m, 15H), 2.66 (s, 6H), 2.65 (s, 3H), 2.08–2.45 (m, 2H), 2.28 (s, 2H), 1.04 (s, 9H).</p>            |
| <p><u>24</u></p> |  | <p><u>914.6</u></p> | <p><sup>1</sup>H NMR (400MHz, MeOD): <math>\delta</math> 8.84 (s, 1H), 8.77 (d, <math>J</math> = 8.0 Hz, 1H), 8.83 (d, <math>J</math> = 8.0 Hz, 1H), 7.57 (d, <math>J</math> = 8.0 Hz, 1H), 7.37–7.45 (m, 5H), 7.24–7.28 (m, 1H), 6.81 (d, <math>J</math> = 8.0 Hz, 1H), 4.86 (s, 1H), 4.50–4.63 (m, 3H), 4.26–4.36 (m, 3H), 3.91–4.03 (m, 4H), 3.86–3.89 (m,</p>                                                                                                                                                  |

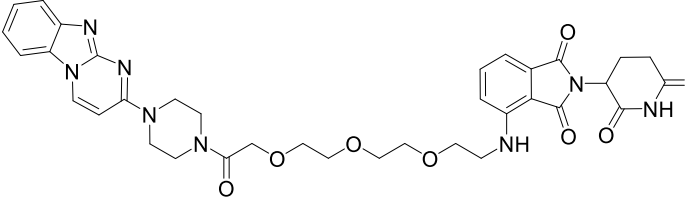
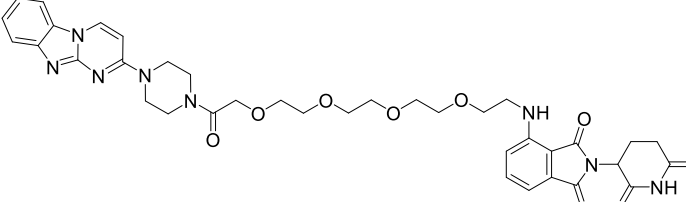
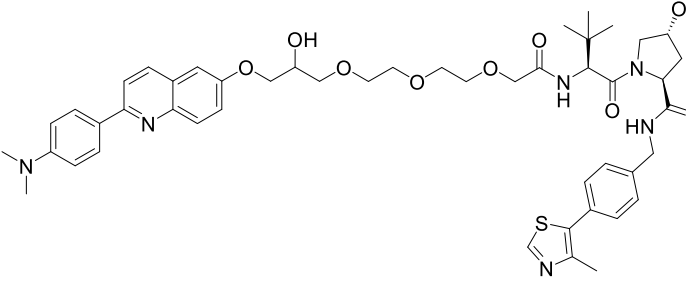
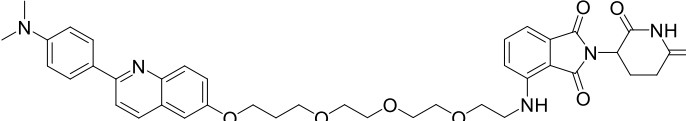
|               |                                                                                                |                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                               |              |
|---------------|------------------------------------------------------------------------------------------------|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|
|               |                                                                                                |                  | <div>2H), 3.74-3.81(m, 2H), 3.60-3.72(m, 16H), 2.45 (s, 3H), 2.18-2.26 (m, 1H), 2.05-2.11 (m, 1H), 1.03 (s, 9H).</div>                                                                                                                                                                                                                                                                                                                                        |              |
| <div>25</div> | <div></div>   | <div>685.4</div> | <div><sup>1</sup>H NMR (400MHz, MeOD): δ 8.68 (d, <i>J</i> = 8.0 Hz, 1H), 7.80 (d, <i>J</i> = 7.2 Hz, 1H), 7.55 (d, <i>J</i> = 8.0 Hz, 1H), 7.39-7.43 (m, 2H), 7.24 (m, <i>J</i> = 7.6 Hz, 1H), 6.95 (t, <i>J</i> = 7.6 Hz, 2H), 6.76 (d, <i>J</i> = 7.6 Hz, 1H), 4.74 (m, 1H), 3.87 (br, 4H), 3.63- 3.73 (m, 14H), 3.54 (s, 3H), 3.46-3.48 (m, 2H), 3.37 (s, 1H), 2.47 (t, <i>J</i> = 6.8 Hz, 2H), 2.33 (t, <i>J</i> = 6.8 Hz, 2H).</div>                    | <div>C</div> |
| <div>26</div> | <div></div> | <div>729.4</div> | <div><sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ 8.65 (d, <i>J</i> = 8.0 Hz, 1H), 7.77 (d, <i>J</i> = 8.0 Hz, 1H ), 7.54 (d, <i>J</i> = 8.0 Hz, 1H ), 7.35-7.4 3 (m, 2H), 7.24 (t, <i>J</i> = 8.0 Hz, 1H), 6.95 (t, <i>J</i> = 8.8 Hz, 2H), 6.75 (d, <i>J</i> = 7.6 Hz, 1H), 5.03 (dd, <i>J</i> = 4.2, 12.4 Hz, 1H), 4.58 (br, 4H), 3.70 (br, 4H), 3.60-3.70 (m, 18H), 3.45-3.46 (m, 2H), 2.80-2.85 (m, 1H), 2.66-2.75 (m, 2H), 2.09-2.12 (m, 1H).</div> | <div>C</div> |
| <div>27</div> | <div></div> | <div>823.7</div> | <div><sup>1</sup>HNMR (400 MHz, CD<sub>3</sub>OD): δ 1.02-1.05 (m, 9H), 2.07-2.13 (m, 1H), 2.21-2.26 (m, 1H), 2.43-2.47 (m, 3H), 3.05 (s, 6H), 3.76-3.83 (m, 5H), 3.88-3.99 (m, 3H), 4.07-4.12 (m, 2H), 4.30-4.35 (m, 3H), 4.47-4.52 (m, 2H), 4.57-4.61 (m, 1H), 4.71-4.73 (m, 1H), 6.87-6.90 (m, 2H), 7.24-7.29 (m, 1H), 7.35-7.43 (m, 5H), 7.70-7.72 (m, 1H), 7.81-7.83 (m, 1H), 7.91-7.96 (m, 3H), 8.14-8.17 (m, 1H), 8.84 (s, 1H).</div>                  | <div>C</div> |

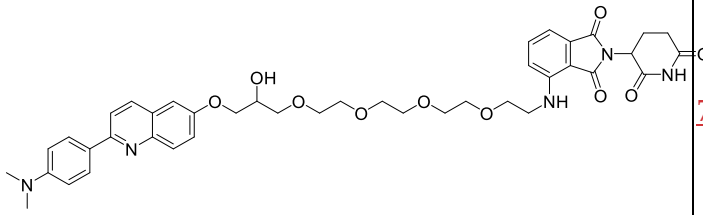
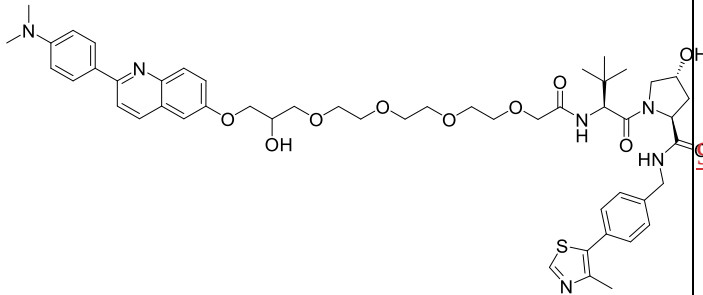
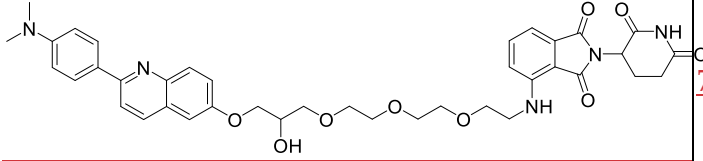
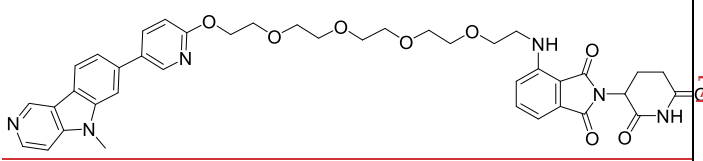
|                  |                                                                                     |                     |                 |
|------------------|-------------------------------------------------------------------------------------|---------------------|-----------------|
| <p><u>28</u></p> |    | <p><u>837.7</u></p> | <p><u>C</u></p> |
| <p><u>29</u></p> |  | <p><u>867.7</u></p> | <p><u>C</u></p> |
| <p><u>30</u></p> |  | <p><u>881.4</u></p> | <p><u>C</u></p> |

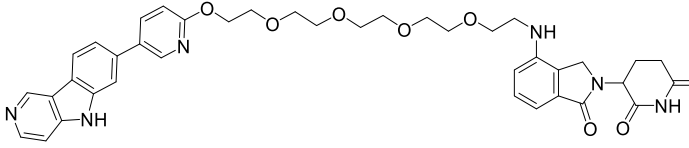
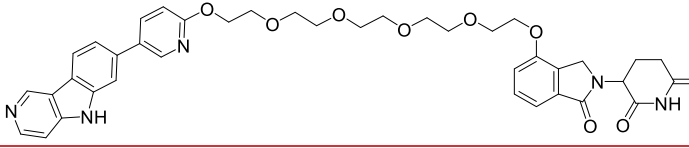
|    |  |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                 |   |
|----|--|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
| 31 |  | 911.4 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 1.04 (s, 9H), 2.07-2.15 (m, 1H), 2.22-2.26 (m, 1H), 2.47 (s, 3H), 3.06 (s, 6H), 3.61-3.75 (s, 12H), 3.82-3.83 (m, 1H), 3.89-3.93 (m, 2H), 4.01-4.07 (m, 2H), 4.28-4.40 (m, 3H), 4.49-4.69 (m, 5H), 6.87-6.97 (m, 2H), 7.27-7.42 (m, 6H), 7.62-7.67 (br, 1H), 7.83-7.98 (m, 4H), 8.17-8.23 (m, 1H), 8.88 (s, 1H).                                                                            | C |
| 32 |  | 925.4 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 1.06 (s, 9H), 1.50-1.58 (m, 3H), 1.94-2.03 (m, 1H), 2.17-2.25 (m, 1H), 2.48 (s, 3H), 3.06 (s, 6H), 3.70-3.77 (m, 12H), 3.85-3.89 (s, 1H), 3.90-4.05 (m, 4H), 4.29-4.35 (m, 2H), 4.43-4.49 (m, 1H), 4.56-4.61 (m, 1H), 4.67-4.71 (m, 1H), 4.99-5.02 (m, 2H), 6.88-6.91 (m, 2H), 7.30-7.41 (m, 5H), 7.63-7.66 (m, 1H), 7.87-7.99 (m, 4H), 8.19-8.23 (m, 1H), 8.50-8.52 (m, 1H), 8.87 (s, 1H). | C |
| 33 |  | 807.4 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 1.05 (s, 9H), 1.89-2.03 (m, 4H), 2.10-2.14 (m, 1H), 2.22-2.26 (m, 1H), 2.46 (s, 3H), 3.05 (s, 6H), 3.67-3.70 (m, 2H), 3.81-3.91 (m, 2H), 3.98-4.09 (m, 2H), 4.17-4.20 (m, 2H), 4.34-4.38 (m, 1H), 4.53-4.62 (m, 3H), 7.71-7.73 (m, 1H), 6.88-6.91 (m, 2H), 7.24-7.28 (m, 1H), 7.34-7.47 (m, 5H), 7.58-7.60 (m, 1H), 7.82-7.84 (m, 1H), 7.91-7.97 (m, 3H), 8.15-8.17 (m, 1H), 8.83 (s, 1H).  | C |

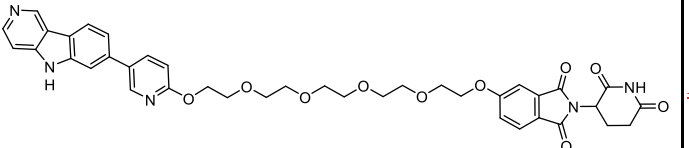


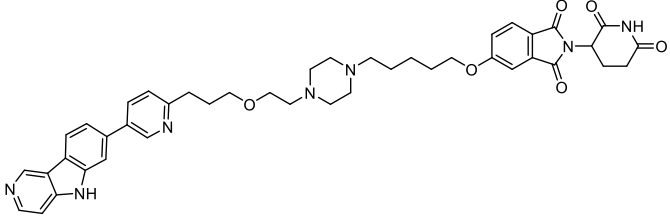
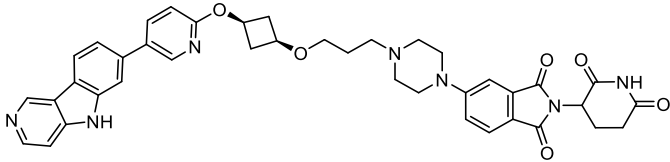
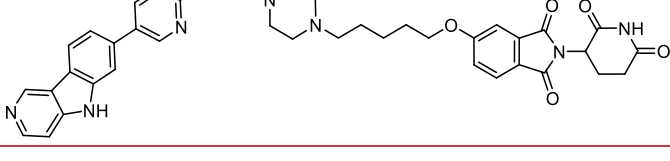
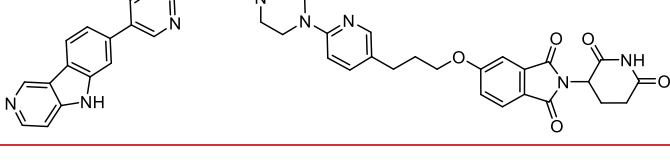
|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
|----|-------------------------------------------------------------------------------------|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
|    |                                                                                     |       | (m, 1H), 3.88-3.91 (m, 1H), 3.96-4.05 (m, 2H), 4.13 (t, <i>J</i> = 6.4 Hz, 2H), 4.32-4.34 (m, 1H), 4.48-4.55 (m, 2H), 4.58-4.63 (m, 1H), 4.69-4.74 (m, 1H), 6.88 (d, <i>J</i> = 8.8 Hz, 2H), 7.20 (s, 1H), 7.33-7.46 (m, 5H), 7.57 (d, <i>J</i> = 9.6 Hz, 1H), 7.81 (d, <i>J</i> = 6.0Hz, 1H), 7.93 (t, <i>J</i> = 10.0 Hz, 3H), 8.14 (d, <i>J</i> = 8.8 Hz, 1H), 8.81 (s, 1H).                                                                                                                                                                                                                               |   |
| 38 |   | 835.4 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.04 (s, 9H), 1.44-1.58 (m, 3H), 1.66-1.81 (m, 4H), 1.89-2.02 (m, 3H), 2.14-2.31 (m, 1H), 2.46 (s, 3H), 3.05 (s, 6H), 3.63 (t, <i>J</i> = 6.4 Hz, 2H), 3.74-3.78 (m, 1H), 3.85-3.88 (m, 1H), 3.96-4.06 (m, 2H), 4.14-4.19 (m, 2H), 4.37-4.46 (m, 1H), 4.56-4.62 (m, 1H), 4.67-4.77 (m, 1H), 4.94-5.04 (m, 1H), 6.89 (d, <i>J</i> = 9.2 Hz, 2H), 7.26 (t, <i>J</i> = 3.2 Hz, 1H), 7.35-7.43 (m, 5H), 7.56 (d, <i>J</i> = 9.6 Hz, 1H), 7.81-7.88 (m, 1H), 8.00-7.91 (m, 3H), 8.18 (d, <i>J</i> = 8.4 Hz, 1H), 8.49 (d, <i>J</i> = 7.2 Hz, 1H), 8.86 (s, 1H). | C |
| 39 |  | 939.4 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.04 (s, 9H), 1.48-1.57 (m, 3H), 1.95-2.22 (m, 5H), 2.47 (s, 3H), 3.06 (s, 6H), 3.60-3.66 (m, 12H), 3.70-3.86 (m, 4H), 3.97-4.06 (m, 2H), 4.24 (t, <i>J</i> = 6.0 Hz, 2H), 4.44 (br, 1H), 4.58 (t, <i>J</i> = 8.4 Hz, 1H), 4.68-4.70 (m, 1H), 4.99-5.02 (m, 1H), 6.89 (d, <i>J</i> = 8.4 Hz, 2H), 7.27 (s, 1H), 7.37-7.43 (m, 5H), 7.61-7.63 (m, 1H), 7.84 (d, <i>J</i> = 8.4 Hz, 1H), 7.95-7.97 (m, 3H), 7.81-7.82 (m, 1H), 8.86(s, 1H).                                                                                                                  | C |
| 40 |  | 754.4 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.92-2.00 (m, 2H), 2.55-2.74 (m, 4H), 2.93 (s, 6H), 3.28-3.37 (m, 4H), 3.46-3.53 (m, 12H), 3.60 (t, <i>J</i> = 6.2 Hz, 2H), 4.11 (t, <i>J</i> = 6.2 Hz, 2H), 4.89-4.93 (m, 1H), 6.41-6.44 (m, 1H), 6.76                                                                                                                                                                                                                                                                                                                                                    | C |

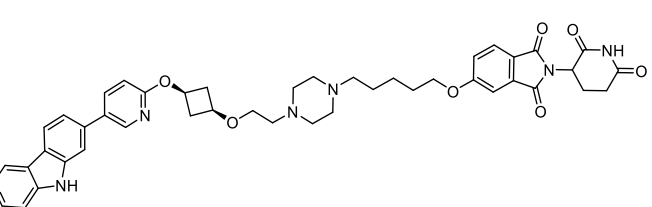
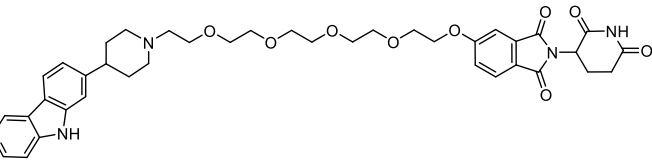
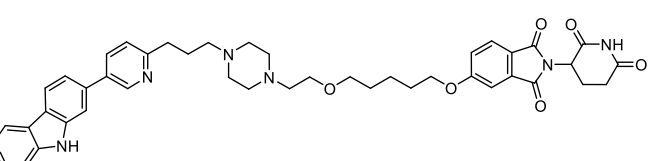
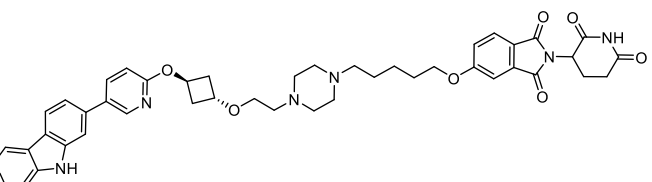
|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |
|----|-------------------------------------------------------------------------------------|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
|    |                                                                                     |       | <p>(d, <math>J = 8.8</math> Hz, 2H), 6.89 (t, <math>J = 7.6</math> Hz, 2H), 7.13 (d, <math>J = 2.4</math> Hz, 1H), 7.23-7.26 (m, 1H), 7.36-7.40 (m, 1H), 7.69 (d, <math>J = 8.8</math> Hz, 1H), 7.80-7.84 (m, 3H), 8.05 (d, <math>J = 8.8</math> Hz, 1H).</p>                                                                                                                                                                                                       |   |
| 41 |    | 699.4 | <p><sup>1</sup>H NMR (400 MHz, MeOD): δ 8.46 (d, <math>J = 8.0</math> Hz, 1H), 7.64 (d, <math>J = 8.0</math> Hz, 1H), 7.45 (d, <math>J = 8.0</math> Hz, 1H), 7.27 (t, <math>J = 7.6</math> Hz, 1H), 7.06-7.14 (m, 2H), 6.57-6.71 (m, 3H), 4.89-4.96 (m, 1H), 4.18 (s, 2H), 3.84 (s, 2H), 3.46-3.70 (m, 16H), 3.30 (s, 2H), 2.58-2.76 (m, 3H), 1.99-2.07 (m, 3H).</p>                                                                                                | C |
| 42 |  | 743.7 | <p><sup>1</sup>H NMR (400MHz, MeOD): δ 8.65 (d, <math>J = 8.0</math> Hz, 1H), 7.77 (d, <math>J = 8.0</math> Hz, 1H), 7.55 (d, <math>J = 8.0</math> Hz, 1H), 7.31-7.40 (m, 2H), 7.21-7.28 (m, 1H), 6.84-7.90 (m, 2H), 6.76 (d, <math>J = 8.0</math> Hz, 1H), 5.00-5.04 (m, 1H), 4.30 (s, 2H), 3.85-3.95 (m, 4H), 3.63-3.70 (m, 18H), 3.38 (s, 2H), 2.61-2.90 (m, 3H), 2.02-2.21 (m, 1H).</p>                                                                         | C |
| 43 |  | 897.4 | <p><sup>1</sup>HNMR (400 MHz, CD<sub>3</sub>OD): δ 1.04 (s, 9H), 2.05-2.13 (m, 1H), 2.21-2.23 (m, 1H), 2.46 (s, 3H), 3.05 (s, 6H), 3.65-3.74 (m, 10H), 3.79-3.90 (m, 2H), 3.98-4.07 (m, 2H), 4.13-4.22 (m, 3H), 4.33-4.37 (m, 1H), 4.50-4.62 (m, 3H), 4.70 (s, 1H), 6.89 (d, <math>J = 8.8</math> Hz, 2H), 7.25-7.26 (m, 1H), 7.38-7.44 (m, 5H), 7.83 (d, <math>J = 8.8</math> Hz, 1H), 7.94-7.97 (m, 3H), 8.17 (d, <math>J = 8.8</math> Hz, 1H), 8.85 (s, 1H).</p> | C |
| 44 |  | 710.3 | <p><sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>): δ 2.07-2.13 (m, 4H), 2.68-2.88 (m, 4H), 3.04 (s, 6H), 3.33-3.45 (m, 2H), 3.64-3.69 (m, 11H), 4.16-4.18 (m, 2H), 4.86-4.90 (m, 1H), 6.42-6.44 (m, 1H), 6.81-6.85 (m, 3H), 7.06-7.07 (m, 2H), 7.32 (d, <math>J = 8.8</math> Hz, 1H), 7.41-7.45 (m, 1H), 7.74-7.77 (m, 1H), 7.98-</p>                                                                                                                                 | C |

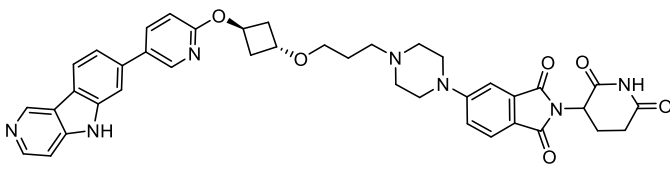
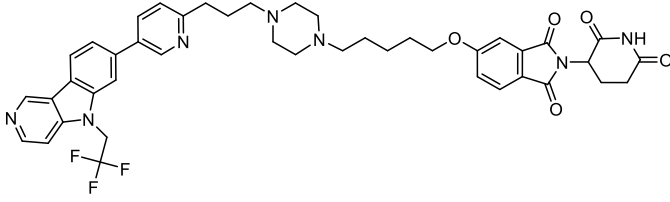
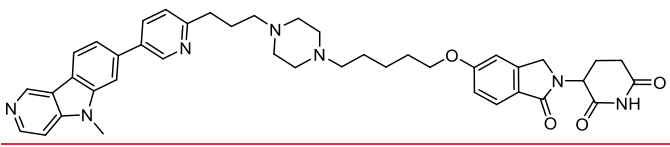
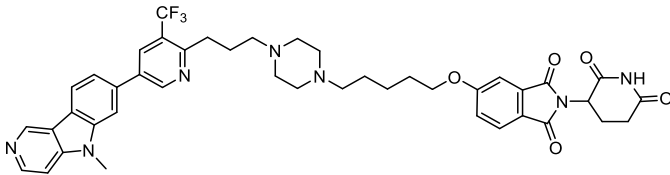
|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |   |
|----|-------------------------------------------------------------------------------------|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
|    |                                                                                     |       | 8.07 (m, 5H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |   |
| 45 |    | 770.3 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 2.07-2.11 (m, 1H), 2.62-2.87 (m, 4H), 3.04 (s, 6H), 3.40-3.43 (m, 2H), 3.65-3.78 (m, 16H), 4.13 (d, <i>J</i> = 5.2 Hz, 2H), 4.24 (t, <i>J</i> = 4.2 Hz, 1H), 4.87-4.91 (m, 1H), 6.45-6.47 (m, 1H), 6.81-6.87 (m, 3H), 7.06, 7.07 (dos singletes, 2H), 7.33-7.36 (m, 1H), 7.44 (t, <i>J</i> = 7.8 Hz, 1H), 7.76 (d, <i>J</i> = 8.8 Hz, 1H), 8.01-8.10 (m, 4H), 8.56 (br. s, 1H).                                                    | C |
| 46 |   | 941.4 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 1.02, 1.04 (dos singletes, 9H), 2.05-2.12 (m, 1H), 2.21-2.27 (m, 1H), 2.46, 2.47 (dos singletes, 3H), 3.07 (s, 6H), 3.63-3.70 (m, 14H), 3.79-3.90 (m, 2H), 3.98-4.07 (m, 2H), 4.13-4.24 (m, 3H), 4.33-4.37 (m, 1H), 4.50-4.61 (m, 3H), 4.69-4.71 (m, 1H), 6.89 (d, <i>J</i> = 8.8 Hz, 2H), 7.33-7.48 (m, 6H), 7.90 (d, <i>J</i> = 8.8 Hz, 1H), 7.97-7.99 (m, 3H), 8.17 (d, <i>J</i> = 8.8 Hz, 1H), 8.87, 8.88 (dos singletes, 1H). | C |
| 47 |  | 726.3 | <sup>1</sup> H NMR (400 Hz, CDCl <sub>3</sub> ): δ 2.01-2.24 (m, 2H), 2.68-2.88 (m, 3H), 3.04 (s, 6H), 3.24 (s, 1H), 3.43 (s, 2H), 3.69 (s, 10H), 4.15-4.24 (m, 3H), 4.83-4.96 (m, 1H), 5.27-5.42 (m, 1H), 6.48 (s, 1H), 6.77-6.83 (m, 3H), 7.07 (s, 2H), 7.34-7.44 (m, 2H), 7.73-7.83 (m, 1H), 7.98-8.05 (m, 4H), 8.27 (s, 1H).                                                                                                                                                       | C |
| 48 |  | 751.2 | <sup>1</sup> H NMR (400 MHz, MeOD): δ 9.24 (s, 1H), 8.50 (d, <i>J</i> = 2.0 Hz, 1H), 8.45 (d, <i>J</i> = 5.6 Hz, 2H), 8.26 (d, <i>J</i> = 8.4 Hz, 1H), 8.06-8.09 (m, 1H), 7.80 (s, 1H), 7.57 (t, <i>J</i> = 8.0 Hz, 2H), 7.44 (t, <i>J</i> = 8.4 Hz, 1H), 6.98 (d, <i>J</i> = 8.4 Hz, 1H), 6.92-6.94 (m, 2H), 4.95-5.09 (m, 1H), 4.49-4.53 (m, 2H), 3.96 (s, 3H), 3.88 (d, <i>J</i> = 4.8 Hz, 2H), 3.63-3.70 (m, 14H), 3.41 (t, <i>J</i> = 6.4                                         | A |

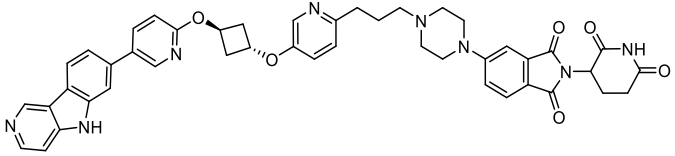
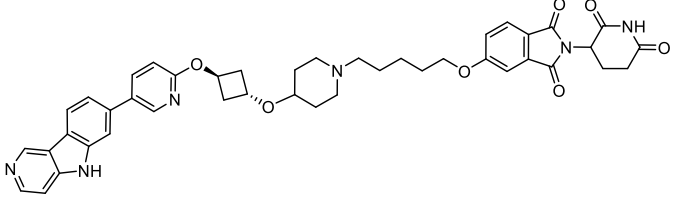
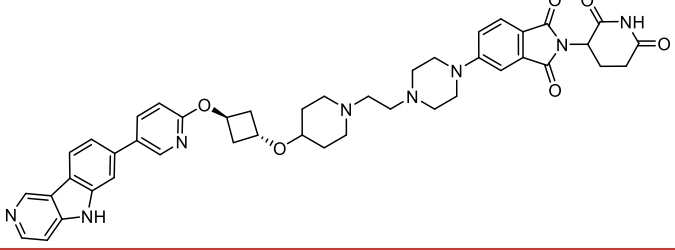
|    |                                                                                                |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |   |
|----|------------------------------------------------------------------------------------------------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
|    |                                                                                                |       | Hz, 2H), 2.64–2.82 (m, 3H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| 49 | <div></div>   | 723.3 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.36 (s, 1H), 8.39-8.45 (m, 3H), 8.30 (d, <i>J</i> = 8.0 Hz, 1H), 8.01 (dd, <i>J</i> = 2.4, 6.4 Hz, 1H), 7.78 (s, 1H), 7.70 (d, <i>J</i> = 6.0 Hz, 1H), 7.59 (d, <i>J</i> = 8.4 Hz, 1H), 7.26 (t, <i>J</i> = 7.6 Hz, 1H), 7.03 (d, <i>J</i> = 7.6 Hz, 1H), 6.90 (d, <i>J</i> = 8.8 Hz, 1H), 6.80 (d, <i>J</i> = 8.0 Hz, 1H), 5.12 (dd, <i>J</i> = 5.2, 13.6 Hz, 1H), 4.47 (t, <i>J</i> = 4.4 Hz, 2H), 4.27 (d, <i>J</i> = 2.4 Hz, 2H), 3.85 (d, <i>J</i> = 4.4 Hz, 2H), 3.62–3.68 (m, 14H), 3.36 (t, <i>J</i> = 5.6 Hz, 2H), 2.75-2.95 (m, 2H), 2.35-2.47 (m, 1H), 2.10-2.21 (m, 1H). | A |
| 50 | <div></div> | 724.3 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 9.29 (s, 1H), 8.52 (s, 1H), 8.36 (s, 1H), 8.13 (d, <i>J</i> = 8.0 Hz, 1H), 7.81 (d, <i>J</i> = 8.0 Hz, 1H), 7.53 (s, 1H), 7.34-7.43 (m, 4H), 6.99 (d, <i>J</i> = 8.4 Hz, 1H), 6.82 (d, <i>J</i> = 8.8 Hz, 1H), 5.16-5.21 (m, 1H), 4.52 (s, 2H), 4.39–4.43 (m, 1H), 4.27-4.31 (m, 1H), 4.18 (d, <i>J</i> = 3.2 Hz, 2H), 3.82-3.89 (m, 4H), 3.64-3.72 (m, 14H), 2.85-2.89 (m, 1H), 2.72–2.81 (m, 1H), 2.27-2.38 (m, 1H), 2.13-2.24 (m, 1H).                                                                                                                                             | A |

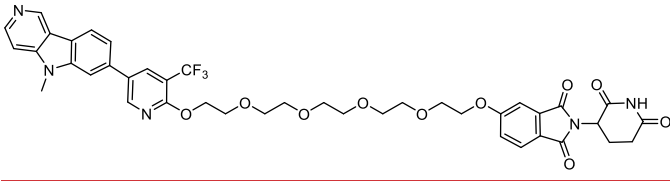
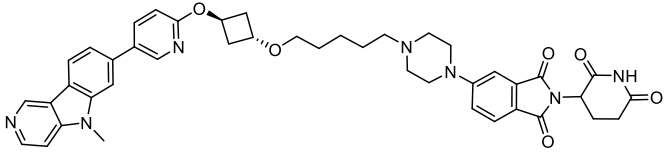
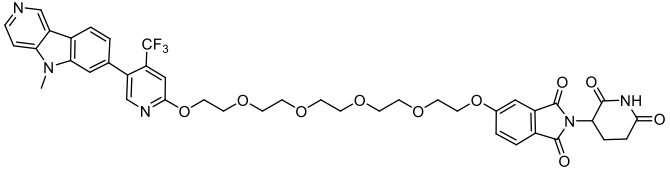
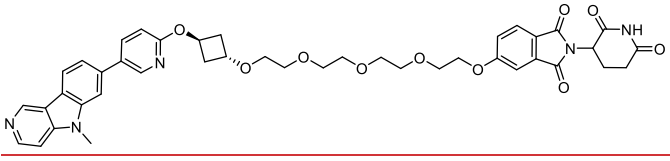
| Ex.<br># | Estructura                                                                                     | Actividad<br>de<br>degrada-<br>ción* | MH+<br>(1)<br>[MH+<br>(2), si<br>isotopo] | transcripto de<br>NMR                                                                                                                                                                                                                                                                                                                                                                   |
|----------|------------------------------------------------------------------------------------------------|--------------------------------------|-------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 51       | <div></div> | A                                    | 738.3                                     | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 12.34–12.48 (m, 1H), 9.19–9.29 (m, 1H), 8.80 (s, 1H), 8.29–8.42 (m, 1H), 8.02–8.14 (m, 1H), 7.95 (s, 1H), 7.69–7.81 (m, 1H), 7.60 (s, 2H), 7.17 (s, 1H), 7.09 (s, 1H), 6.62 (s, 1H), 4.97 (s, 1H), 4.43 (s, 2H), 4.14 (s, 2H), 3.88 (d, <i>J</i> = 24.1 Hz, 3H), 3.78 (d, <i>J</i> = 8.2 Hz, 3H), 3.69 (d, <i>J</i> = 10.0 Hz, 6H). |

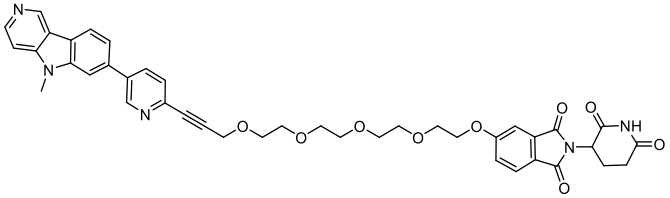
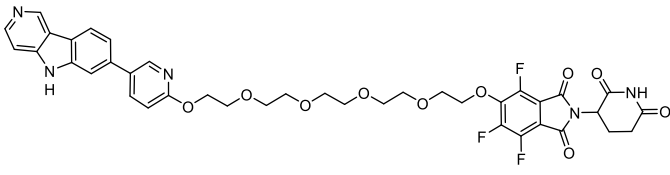
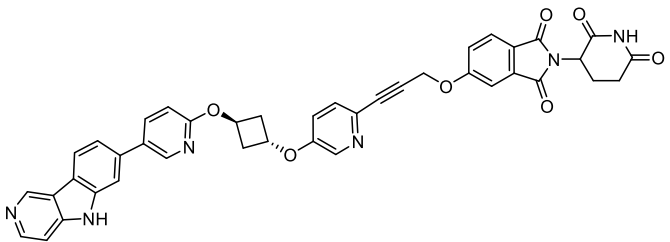
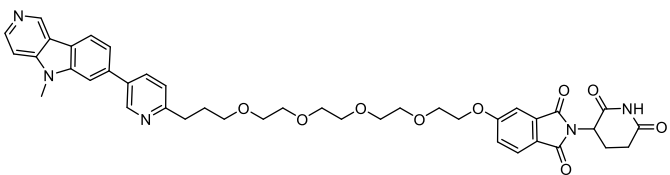
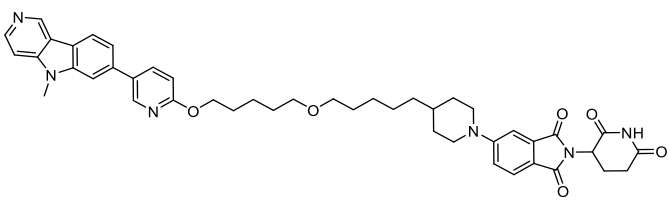
|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|----|-------------------------------------------------------------------------------------|---|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                     |   |       | 2.80 (m, 4H), 1.99 – 2.29 (m, 4H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| 52 |    | C | 758.3 | <sup>1</sup> HNMR (400 MHz, MeOD):<br>$\delta$ 9.25 (s, 1H), 8.79 (s, 1H), 8.37-8.39 (d, $J$ =8 Hz, 1H), 8.28-8.30 (d, $J$ =8 Hz, 1H), 8.11-8.13 (d, $J$ =8 Hz, 1H), 7.80 (s, 1H), 7.75-7.77 (d, $J$ =8 Hz, 1H), 7.60 (s, 1H), 7.49-7.51 (d, $J$ =8 Hz, 1H), 7.43-7.45 (d, $J$ =8 Hz, 1H), 7.33 (s, 1H), 5.07-5.09 (m, 1H), 4.06-4.09 (m, 2H), 3.57-3.60 (m, 2H), 3.51-3.54 (m, 2H), 2.93-2.95 (m, 2H), 2.91-2.93 (m, 1H), 2.59-2.75 (m, 12H), 2.37-2.41 (m, 2H), 2.04-2.06 (m, 3H), 1.78-1.80 (m, 2H), 1.46-1.55 (m, 5H). |
| 53 |  | C | 714.3 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ):<br>$\delta$ 9.34 (s, 1H), 8.55 (d, $J$ =5.6 Hz, 1H), 8.44 (m, 2H), 8.20 (d, $J$ =8.4 Hz, 1H), 7.87-7.92 (m, 3H), 7.68 (d, $J$ =8.4 Hz, 1H), 7.60 (s, 1H), 7.48-7.50 (m, 1H), 7.38 (d, $J$ =5.6 Hz, 1H), 7.06 (m, 1H), 6.84 (d, $J$ =8.8 Hz, 2H), 4.93-4.94 (m, 2H), 3.75 (m, 2H), 3.42-3.49 (m, 6H), 2.72-2.98 (m, 5H), 2.61 (s, 4H), 2.53 (t, $J$ =7.2 Hz, 2H), 2.15-2.18 (m, 2H), 1.81 (t, $J$ =6.8 5Hz, 2H).                                                          |
| 54 |  | C | 714.3 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): $\delta$ 9.31 (s, 1H), 8.83 (s, 1H), 8.42 (d, $J$ =6.1 Hz, 2H), 8.34 (d, $J$ =8.3 Hz, 1H), 8.14 (d, $J$ =8.0 Hz, 1H), 7.84 (s, 1H), 7.78 (d, $J$ =8.5 Hz, 1H), 7.61 (dd, $J$ =16.5, 6.4 Hz, 2H), 7.47 (d, $J$ =8.3 Hz, 1H), 7.36 (s, 1H), 7.28 (d, $J$ =8.2 Hz, 1H), 5.06 – 5.13 (m, 1H), 4.14 (s, 2H), 2.83 (m, 18H), 2.04 (s, 3H), 1.87 (s, 2H), 1.69 (s, 2H), 1.55 (s, 2H).                                                                                           |
| 55 |  | C | 763.3 | <sup>1</sup> H NMR (400 MHz, MeOD):<br>$\delta$ 9.62 (s, 1H), 9.03 (s, 1H), 8.58 (d, $J$ =6.8 Hz, 1H), 8.52 (d, $J$ =8.0 Hz, 1H), 8.31-8.40 (m, 1H), 8.08 (s, 1H), 7.87-7.99 (m, 2H), 7.78-7.87 (m, 3H), 7.68-7.72 (m, 1H), 7.26-7.30 (m, 2H), 7.10-7.14 (m, 1H), 5.08-5.12 (m, 1H), 4.17 (t, $J$ =6.0 Hz, 2H), 3.81-3.92 (m, 4H), 3.50-3.60 (m, 4H), 3.30-3.40 (m, 2H), 3.10-3.18 (m, 2H), 2.71-2.86 (m, 5H), 2.30-2.33 (m, 2H), 2.10-2.16 (m, 3H).                                                                       |

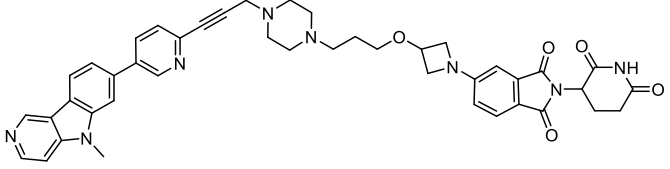
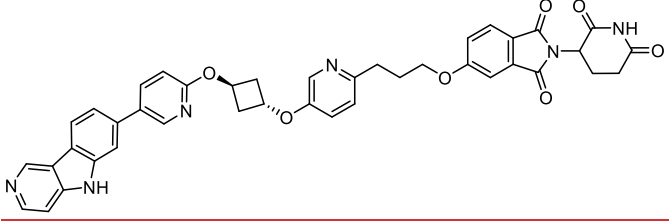
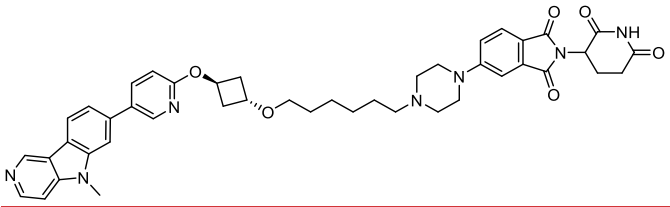
|    |                                                                                     |   |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|----|-------------------------------------------------------------------------------------|---|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 56 |    | C |  | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ) δ 9.33 (s, 1H), 8.89 (s, 1H), 8.53 (s, 1H), 8.42 (s, 1H), 8.18 (d, <i>J</i> = 8.2 Hz, 1H), 7.87 (d, <i>J</i> = 6.2 Hz, 1H), 7.77 (d, <i>J</i> = 8.2 Hz, 1H), 7.62 (s, 1H), 7.49 (d, <i>J</i> = 7.7 Hz, 1H), 7.42 (s, 1H), 7.29 (d, <i>J</i> = 11.5 Hz, 1H), 7.17 (d, <i>J</i> = 6.5 Hz, 1H), 6.82 (d, <i>J</i> = 8.2 Hz, 1H), 5.34 (s, 2H), 5.00 – 4.87 (m, 1H), 4.07 (s, 2H), 3.75 (s, 1H), 3.57 (s, 1H), 3.04 – 2.49 (m, 10H), 2.20 (m, 4H), 2.01 (s, 4H), 1.85 (s, 3H), 1.75 – 1.55 (m, 3H), 1.52 (s, 2H).                                                                                                               |
| 57 |   | C |  | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.30 (s, 1H), 8.42-8.60 (m, 2H), 8.19 (d, <i>J</i> =8.0 Hz, 1H), 7.60-7.65 (m, 2H), 7.52 (s, 1H), 7.31 (d, <i>J</i> = 8.0 Hz, 1H), 7.19 (s, 1H), 7.12-7.14 (m, 1H), 5.07-5.10 (m, 1H), 4.12 (t, <i>J</i> = 4.0 Hz, 2H), 3.66-3.86 (m, 18H), 3.37 (s, 2H), 3.15-3.20 (m, 3H), 2.71-2.76 (m, 3H), 2.09-2.22 (m, 5H).                                                                                                                                                                                                                                                                                                       |
| 58 |  | C |  | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.25 (s, 1H), 8.79 (s, 1H), 8.39 (d, <i>J</i> = 6.0 Hz, 1H), 8.30 (d, <i>J</i> = 8.0 Hz, 1H), 8.12 (d, <i>J</i> = 8.0 Hz, 1H), 7.79 (s, 1H), 7.76 (d, <i>J</i> = 8.4 Hz, 1H), 7.59 (d, <i>J</i> = 8.0 Hz, 1H), 7.52 (d, <i>J</i> = 5.2 Hz, 1H), 7.44 (d, <i>J</i> = 8.0 Hz, 1H), 7.35 (d, <i>J</i> = 6.0 Hz, 1H), 5.07-5.09 (m, 1H), 4.13 (t, <i>J</i> = 6.4 Hz, 2H), 3.59 (t, <i>J</i> = 5.2 Hz, 2H), 3.47 (t, <i>J</i> = 6.0 Hz, 2H), 2.47-2.88 (m, 16H), 1.98-2.1 (m, 4H), 1.80-1.84 (m, 2H), 1.55-1.57 (m, 5H).                                                                                                      |
| 59 |  | C |  | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ 11.79 (s, 1H), 11.11 (s, 1H), 9.35 (s, 1H), 8.55 (s, 1H), 8.42 (d, <i>J</i> = 5.4 Hz, 1H), 8.29 (d, <i>J</i> = 8.2 Hz, 1H), 8.17 (s, 1H), 8.11 (d, <i>J</i> = 8.6 Hz, 1H), 7.82 (d, <i>J</i> = 8.6 Hz, 1H), 7.76 (s, 1H), 7.55 (d, <i>J</i> = 8.2 Hz, 1H), 7.48 (d, <i>J</i> = 5.6 Hz, 1H), 7.42 (s, 1H), 7.34 (d, <i>J</i> = 8.0 Hz, 1H), 6.93 (d, <i>J</i> = 8.6 Hz, 1H), 5.31 (s, 1H), 5.11 (dd, <i>J</i> = 12.9, 5.2 Hz, 1H), 4.17 (d, <i>J</i> = 6.7 Hz, 3H), 3.42 (d, <i>J</i> = 5.4 Hz, 2H), 2.96 – 2.78 (m, 2H), 2.60 (dd, <i>J</i> = 34.5, 18.5 Hz, 2H), 2.37 (dd, <i>J</i> = 44.1, 5.8 Hz, 13H), 2.01 |

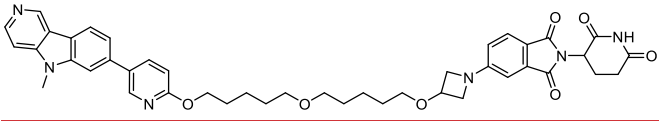
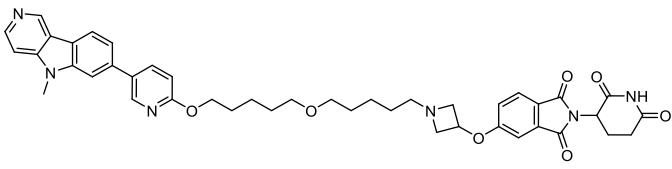
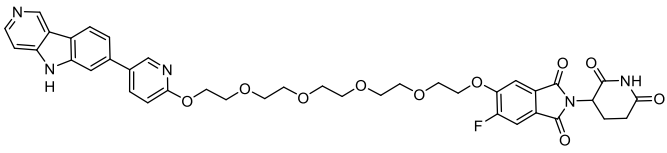
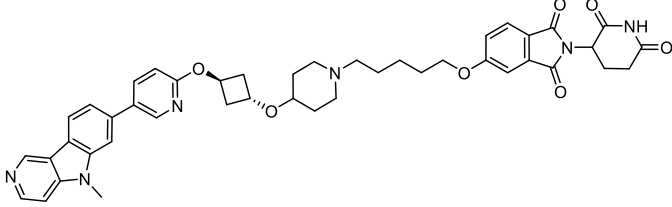
|           |                                                                                     |          |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-----------|-------------------------------------------------------------------------------------|----------|--------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|           |                                                                                     |          |              | (d, $J$ = 14.9 Hz, 2H), 1.76 (s, 2H), 1.41 (dd, $J$ = 43.8, 29.4 Hz, 4H), 1.23 (s, 2H).                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <u>60</u> |    | <u>C</u> | <u>714.3</u> | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 11.07 (s, 1H), 9.76 (s, 1H), 8.67 (d, $J$ = 6.0 Hz, 1H), 8.60 (s, 1H), 8.52 (d, $J$ = 8.4 Hz, 1H), 8.16 (d, $J$ = 8.4 Hz, 1H), 8.80-8.02 (m, 2H), 7.77 (t, $J$ = 8.4 Hz, 2H), 7.50 (s, 1H), 7.37 (d, $J$ = 8.0 Hz, 1H), 6.96 (d, $J$ = 8.8 Hz, 1H), 5.36 (m, 1H), 5.07-5.11 (m, 1H), 4.24 (br, 3H), 3.62 (br, 9H), 3.55 (s, 3H), 3.17-3.25 (m, 6H), 2.86-2.93 (m, 1H), 2.38-2.62 (m, 4H), 1.97-2.04 (m, 1H).                                                |
| <u>61</u> |  | <u>C</u> | <u>796.3</u> | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD) δ 9.35 (s, 1H), 8.89 (s, 1H), 8.55 (d, $J$ = 5.8 Hz, 1H), 8.40 (d, $J$ = 8.0 Hz, 1H), 8.17 – 8.22 (m, 1H), 8.05 (s, 1H), 7.81 (d, $J$ = 8.3 Hz, 1H), 7.74 (d, $J$ = 5.6 Hz, 1H), 7.51 (d, $J$ = 8.2 Hz, 1H), 7.40 (s, 1H), 7.33 (s, 1H), 5.40 (d, $J$ = 9.1 Hz, 2H), 5.08 – 5.16 (m, 1H), 4.95 (s, 4H), 4.59 (s, 2H), 4.18 (t, $J$ = 6.2 Hz, 1H), 2.91 – 3.00 (m, 2H), 2.58 – 2.91 (m, 9H), 2.12 – 2.18 (m, 1H), 2.06 (s, 2H), 1.89 (s, 2H), 1.69 (s, 2H), 1.57 (s, 2H). |
| <u>62</u> |  | <u>C</u> | <u>714.3</u> | <sup>1</sup> H NMR (400 MHz, MeOD): δ 9.27 (s, 1H), 8.86 (d, $J$ = 2.0 Hz, 1H), 8.46 (d, $J$ = 6.0 Hz, 1H), 8.33 (d, $J$ = 8.0 Hz, 1H), 8.16 (d, $J$ = 2.4 Hz, 1H), 7.90 (s, 1H), 7.59-7.70 (m, 3H), 7.47 (d, $J$ = 6.0 Hz, 1H), 7.03-7.09 (m, 2H), 5.06-5.12 (m, 1H), 4.42 (d, $J$ = 5.6 Hz, 2H), 4.07 (t, $J$ = 6.4 Hz, 2H), 3.99 (s, 3H), 2.89-2.96 (m, 3H), 2.51-2.75 (m, 13H), 2.12-2.24 (m, 1H), 2.01-2.03 (m, 3H), 1.82-1.84 (m, 2H), 1.52-1.63 (m, 6H).                                                           |
| <u>63</u> |  | <u>C</u> | <u>796.2</u> | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.25 (s, 1H), 8.45 (s, 1H), 8.23 (d, $J$ = 7.6 Hz, 1H), 7.76 (d, $J$ = 8.4 Hz, 1H), 7.66 (s, 1H), 7.59 (d, $J$ = 8.0 Hz, 1H), 7.39 (d, $J$ = 8.4 Hz, 1H), 7.35 (s, 2H), 7.26-7.28 (m, 1H), 6.06 (s, 1H), 5.72 (s, 1H), 5.06–5.08 (m, 1H), 4.30 (d, $J$ = 6.4 Hz, 1H), 4.11–4.15 (m, 2H), 3.90–3.94 (m, 4H), 3.70–3.74 (m, 2H).                                                                                                                                        |

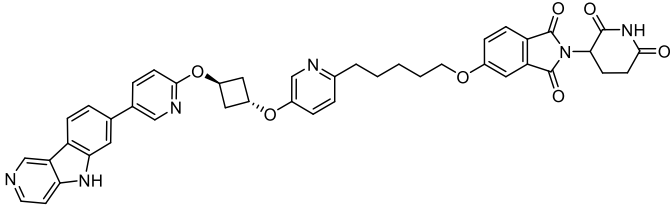
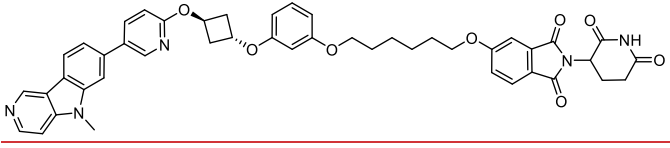
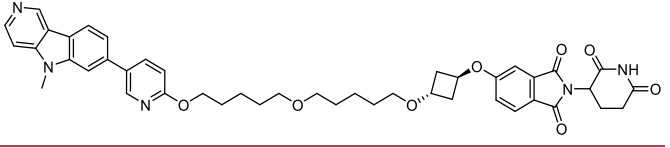
|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|----|-------------------------------------------------------------------------------------|---|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                     |   |       | 3.03–3.06 (m, 2H), 2.82–2.88 (m, 4H), 2.71–2.75 (m, 6H), 2.51–2.55 (m, 3H), 2.05–2.25 (m, 2H), 1.82–1.86 (m, 2H), 1.61–1.63 (m, 2H), 1.51–1.52 (m, 2H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| 64 |    | C | 791.2 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD) δ 9.42 (s, 1H), 8.53 (d, <i>J</i> = 2.3 Hz, 1H), 8.50 (d, <i>J</i> = 6.1 Hz, 1H), 8.38 (d, <i>J</i> = 8.1 Hz, 1H), 8.13 (d, <i>J</i> = 8.0 Hz, 2H), 7.87 (s, 1H), 7.71–7.78 (m, 2H), 7.68 (d, <i>J</i> = 8.3 Hz, 1H), 7.42 (s, 1H), 7.33 (s, 2H), 7.29 (d, <i>J</i> = 8.6 Hz, 1H), 6.99 (d, <i>J</i> = 8.6 Hz, 1H), 5.51 (s, 2H), 5.06–5.14 (m, 2H), 3.55 (s, 4H), 2.58–3.03 (m, 15H), 2.04 (m, 3H).                                                                                                                                                                                                                                                                                                                     |
| 65 |  | C | 757.5 | <sup>1</sup> H NMR: (400 MHz, DMSO-d <sub>6</sub> ) δ : 11.80 (s, 1H), 11.11 (s, 1H), 9.35 (s, 1H), 8.55 (d, <i>J</i> =2.4 Hz, 1H), 8.42 (d, <i>J</i> =5.6 Hz, 1H), 8.29 (d, <i>J</i> =8.4 Hz, 1H), 8.18 (s, 3H), 8.11 (dd, <i>J</i> =2.4, 8.8 Hz, 1H), 7.83 (d, <i>J</i> =8.4 Hz, 1H), 7.76 (s, 1H), 7.55 (d, <i>J</i> =8.4 Hz, 1H), 7.48 (d, <i>J</i> =5.6 Hz, 1H), 7.42 (d, <i>J</i> =2.0 Hz, 1H), 7.35 (dd, <i>J</i> =2.0, 8.4 Hz, 1H), 6.92 (d, <i>J</i> =8.4 Hz, 1H), 5.30 (d, <i>J</i> =3.6 Hz, 1H), 5.11 (dd, <i>J</i> =5.6, 13.2 Hz, 1H), 4.35 (t, <i>J</i> =6.4 Hz, 1H), 4.17 (t, <i>J</i> =6.4 Hz, 2H), 2.93 - 2.84 (m, 2H), 2.77 (s, 2H), 2.63 - 2.54 (m, 3H), 2.37 (d, <i>J</i> =6.0 Hz, 4H), 2.22 - 1.98 (m, 4H), 1.87 - 1.74 (m, 4H), 1.53 - 1.38 (m, 6H). |
| 66 |  | C | 783.6 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 13.21 (s, 1H), 11.08 (s, 2H), 9.76 (s, 1H), 8.67 (d, <i>J</i> = 6.6 Hz, 1H), 8.61 (s, 1H), 8.52 (d, <i>J</i> = 8.3 Hz, 1H), 8.17 (d, <i>J</i> = 8.3 Hz, 1H), 8.02 (d, <i>J</i> = 7.1 Hz, 2H), 7.82 – 7.72 (m, 3H), 7.46 (s, 2H), 7.35 (s, 2H), 6.96 (d, <i>J</i> = 8.5 Hz, 1H), 5.34 (s, 1H), 5.08 (d, <i>J</i> = 7.7 Hz, 2H), 4.40 (s, 2H), 3.23 (s, 4H), 3.15 (s, 4H), 3.02 (s, 4H), 2.95 – 2.83 (m, 4H), 2.59 (d, <i>J</i> = 15.7 Hz, 4H), 2.44 (s, 2H), 2.01 (s, 5H), 1.77 (d, <i>J</i> = 14.7 Hz, 2H).                                                                                                                                                                                                         |

|    |                                                                                     |          |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|----|-------------------------------------------------------------------------------------|----------|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 67 |    | <u>A</u> | 820.5 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.25 (s, 1H), 8.79 (s, 1H), 8.37–8.39 (d, <i>J</i> = 8.0 Hz, 1H), 8.28–8.30 (d, <i>J</i> = 8.0 Hz, 2H), 7.89 (s, 1H), 7.63–7.65 (d, <i>J</i> = 8.0 Hz, 1H), 7.54–7.56 (m, 2H), 7.26 (s, 1H), 7.18–7.20 (m, 1H), 5.02–5.05 (m, 1H), 4.62–4.64 (m, 2H), 4.17–4.19 (m, 2H), 3.95 (s, 3H), 3.88–3.90 (m, 2H), 3.82–3.84 (m, 2H), 3.61–3.71 (m, 13H), 2.55–2.81 (m, 3H), 2.95–2.99 (m, 1H).                                                                                                                                                                            |
| 68 |   | <u>C</u> | 756.6 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 11.12 (s, 1H), 9.37 (s, 1H), 8.64 (s, 1H), 8.50 (d, <i>J</i> = 4.0 Hz, 1H), 8.33 (d, <i>J</i> = 12.0 Hz, 1H), 8.00 (s, 1H), 7.68–7.60 (m, 3H), 7.34 (d, <i>J</i> = 4.0 Hz, 1H), 7.25 (dd, <i>J</i> = 8.0 Hz, 4.0 Hz, 1H), 6.94 (d, <i>J</i> = 8.0 Hz, 1H), 5.32 (t, <i>J</i> = 4.0 Hz, 1H), 5.07 (dd, <i>J</i> = 12.0 Hz, 8.0 Hz, 1H), 4.20–4.17 (m, 1H), 3.96 (s, 3H), 4.46 (s, 6H), 2.88–2.84 (m, 1H), 2.59–2.54 (m, 7H), 2.43–2.32 (m, 6H), 2.02–1.98 (m, 1H), 1.57–1.49 (m, 4H), 1.38–1.34 (m, 2H).                                                 |
| 69 |  | <u>A</u> | 820.5 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.21 (s, 1H), 8.79 (s, 1H), 8.38 (d, <i>J</i> = 8.0 Hz, 2H), 7.62 (d, <i>J</i> = 8.0 Hz, 1H), 7.46–7.49 (m, 2H), 7.26 (s, 1H), 7.15–7.19 (m, 2H), 7.07 (s, 1H), 4.95–4.99 (m, 1H), 4.45–4.47 (m, 2H), 4.15–4.18 (m, 2H), 3.77–3.82 (m, 7H), 3.54–3.62 (m, 9H), 2.45–2.77 (m, 3H), 1.91–1.95 (m, 1H), 1.12–1.16 (m, 1H).                                                                                                                                                                                                                                           |
| 70 |  | <u>A</u> | 778.5 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 11.10 (s, 1H), 9.36 (s, 1H), 8.62 (s, 1H), 8.50 (s, 1H), 8.31 (d, <i>J</i> = 8.2 Hz, 1H), 8.18 (d, <i>J</i> = 8.8 Hz, 1H), 7.97 (s, 1H), 7.81 (d, <i>J</i> = 8.3 Hz, 1H), 7.60 (d, <i>J</i> = 8.0 Hz, 2H), 7.43 (s, 1H), 7.35 (d, <i>J</i> = 7.8 Hz, 1H), 6.93 (d, <i>J</i> = 8.7 Hz, 1H), 5.31 (s, 1H), 5.11 (dd, <i>J</i> = 12.8, 5.1 Hz, 1H), 4.31 (s, 2H), 4.22 (s, 1H), 3.95 (s, 3H), 3.79 (s, 2H), 3.64–3.48 (m, 10H), 3.45 (d, <i>J</i> = 4.9 Hz, 3H), 2.86 (d, <i>J</i> = 13.2 Hz, 1H), 2.45–2.40 (m, 2H), 2.37–2.30 (m, 2H), 2.02 (d, <i>J</i> |

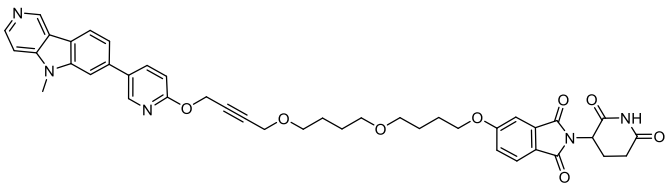
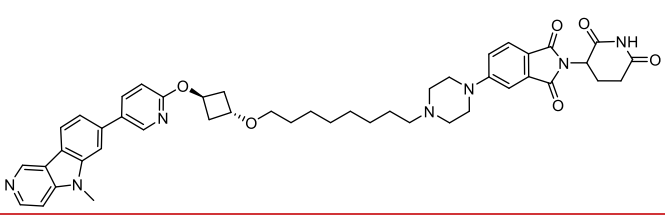
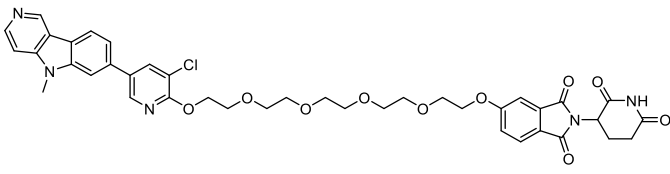
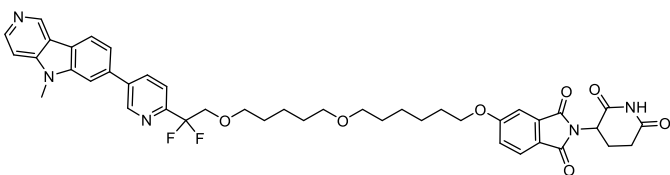
|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|----|-------------------------------------------------------------------------------------|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                     |   |       | = 6.5 Hz, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 71 |    | A | 746.5 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 9.39 (s, 1H), 8.38 (d, <i>J</i> = 8.4 Hz, 1H), 8.30 (d, <i>J</i> = 2.0 Hz, 1H), 8.28 (d, <i>J</i> = 3.0 Hz, 1H), 8.11 (s, 1 H), 7.80 (d, <i>J</i> = 8.4 Hz, 1H), 7.72 (d, <i>J</i> = 7.6 Hz, 1H), 7.63–7.68 (m, 2H), 7.44 (d, <i>J</i> = 2.0 Hz, 1H), 7.34–7.36 (m, 1H), 5.08–5.12 (m, 1H), 4.48 (s, 2H), 4.31 (t, <i>J</i> = 3.6 Hz, 2H), 3.98 (s, 3H), 3.80 (s, 3H), 3.53–3.79 (m, 12H), 1.95–2.08 (m, 2H). |
| 72 |   | C | 792.5 | <sup>1</sup> H NMR(400 MHz, CD <sub>3</sub> OD): δ 13.19 (s, 1H), 9.77 (s, 1H), 8.62–8.68 (m, 2H), 8.52 (d, <i>J</i> = 8.0 Hz, 1H), 8.16 (s, 1H), 8.01–8.02 (m, 2H), 7.80–7.81 (m, 1H), 7.15–7.28 (m, 1H), 6.99 (d, <i>J</i> = 8.0 Hz, 1H), 5.15–5.23 (m, 1H), 4.43–4.45 (m, 2H), 3.77–3.89 (m, 4H), 3.49–3.60 (m, 12H), 2.86–3.05 (m, 3H), 1.99–2.01 (m, 1H).                                                                                                              |
| 73 |  | A | 719.4 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 2.04-2.07 (m, 1H), 2.57-2.77 (m, 6H), 2.86-2.93 (m, 1H), 5.10-5.14 (m, 2H), 5.32 (s, 2H), 5.39-5.48 (m, 1H), 6.97 (d, <i>J</i> = 8.0 Hz, 1H), 7.32-7.33 (m, 1H), 7.46-7.58 (m, 5H), 7.77 (s, 1H), 7.90 (d, <i>J</i> = 7.2 Hz, 1H), 8.14 (d, <i>J</i> = 7.2 Hz, 1H), 8.25 (s, 1H), 8.30 (d, <i>J</i> = 7.6 Hz, 1H), 8.43 (s, 1H), 8.56 (s, 1H), 9.36 (s, 1H), 11.12 (s, 1H), 11.82 (s, 1H).                    |
| 74 |  | A | 750.5 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 9.65 (s, 1H), 9.22 (s, 1H), 8.67–8.73 (m, 2H), 8.47 (d, <i>J</i> = 7.6 Hz, 1H), 8.36 (d, <i>J</i> = 8.0 Hz, 1H), 7.97 (s, 1 H), 7.83 (s, 1H), 7.81(s, 1H), 7.59–7.71 (m, 2H), 7.04 (d, <i>J</i> = 9.2 Hz, 2H), 4.93–4.96 (m, 1H), 4.10 (s, 5H), 3.87 (s, 1H), 3.55–3.76 (m, 18H), 3.26 (s, 2H), 2.12–2.16 (m, 2H).                                                                                                      |
| 75 |  | C | 771.6 | <sup>1</sup> H NMR (400MHz, DMSO- <i>d</i> <sub>6</sub> )<br>δ = 11.07 (s, 1H), 9.38 - 9.32 (m, 1H), 8.66 - 8.63 (d, <i>J</i> = 12 Hz 1H), 8.50 - 8.48 (m, <i>J</i> = 8 Hz 1H), 8.36 (s, 2H), 8.34 - 8.29 (m, 1H), 8.21 - 8.14 (m, 1H), 7.99 - 7.94 (m, 1H), 7.61 (s, 3H), 7.28 - 7.22                                                                                                                                                                                      |

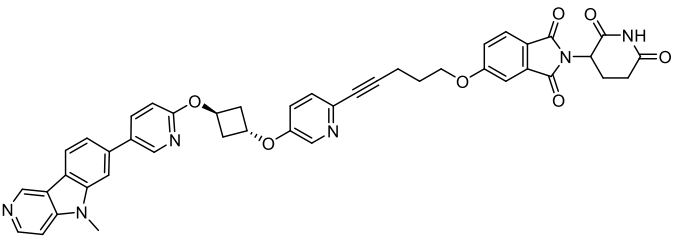
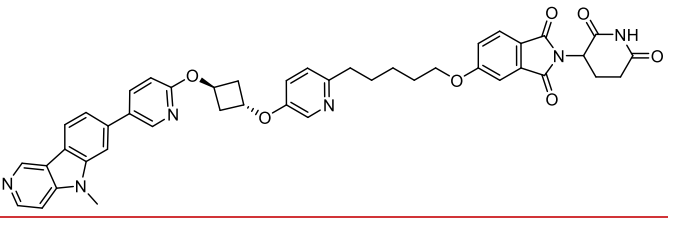
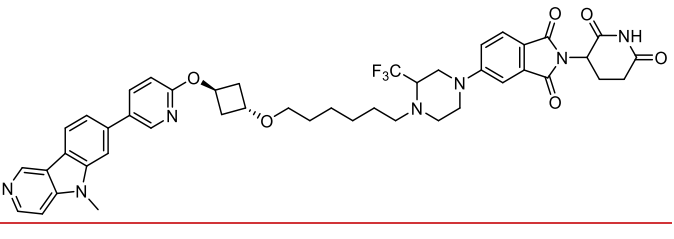
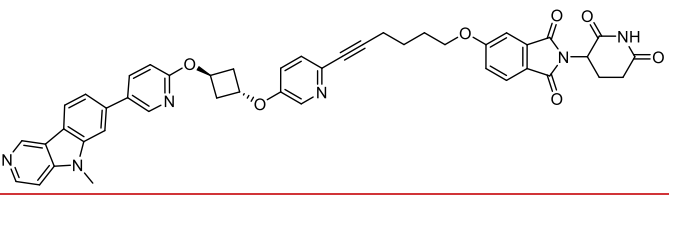
|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|----|-------------------------------------------------------------------------------------|---|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                     |   |       | (m, 1H), 7.19 - 7.12 (m, 1H),<br>6.96 - 6.89 (m, 1H), 5.09 -<br>5.00 (m, 1H), 4.36 - 4.29 (m,<br>2H), 3.95 (s, 5H), 3.34 ( s,<br>4H), 2.87 ( s, 2H), 2.99 - 2.78<br>(m, 1H), 2.82 - 2.73 (m, 1H),<br>2.04 - 1.93 (m, 1H), 1.82 -<br>1.65 (m, 4H), 1.61 - 1.52 (m,<br>2H), 1.52 - 1.41 (m, 5H),<br>1.28 ( s, 4H), 1.22 - 1.05 (m,<br>4H).                                                                                                                                                                                                                                                                                                                                                              |
| 76 |    | C | 751.5 | <sup>1</sup> H NMR (400 MHz,<br>CD <sub>3</sub> OD): δ 9.32 (s, 1H), 8.96<br>(s, 1H), 8.45-8.52 (m, 2H),<br>8.37 (d, <i>J</i> = 8.0 Hz, 1H),<br>8.27-8.31(m, 1H), 7.98 (s,<br>1H), 7.61-7.98 (m, 4H), 6.82<br>(s, 1H), 6.65-6.67 (m, 1H),<br>5.01-5.05 (m, 1H), 4.59 (m,<br>1H), 4.27 (t, <i>J</i> = 8.4 Hz, 1H),<br>4.02 (s, 3H), 3.88-3.91 (m,<br>2H), 3.70 (s, 2H), 3.57(t, <i>J</i> =<br>6.0 Hz, 2H), 3.41(m, 1H),<br>3.13-3.17 (m, 2H), 2.66-2.86<br>(m, 11H), 2.02-2.03 (m, 3H).                                                                                                                                                                                                                |
| 77 |  | C | 723.5 | <sup>1</sup> H NMR (400 MHz,<br>CD <sub>3</sub> OD): δ 9.56 (s,1H),<br>8.54–8.56 (m, 2H), 8.45 (d, <i>J</i><br>= 8.4 Hz, 1H), 8.37 (d, <i>J</i> =<br>2.4 Hz, 1H), 8.13 (d, <i>J</i> = 8.0<br>Hz, 1H), 7.97 (d, <i>J</i> = 8.0 Hz,<br>1H), 7.88 (d, <i>J</i> = 8.8 Hz, 2H),<br>7.81 (d, <i>J</i> = 8.4 Hz, 1H), 7.79<br>(s, 1H), 7.76–7.78 (d, <i>J</i> = 8<br>Hz, 1H), 7.29 (s, 1H), 7.21(d,<br><i>J</i> = 8.0 Hz, 1H), 6.98(d, <i>J</i> =<br>8.0 Hz, 1H), 5.48–5.52 (m,<br>1H), 5.32–5.34 (m, 1H),<br>5.18–5.22 (m, 1H), 5.06–<br>5.10 (m, 1H), 4.25–4.28 (m,<br>2H), 3.21–3.23 (m, 3H),<br>2.78–2.81 (m, 5H), 2.67–<br>2.70 (m, 2H), 2.30–2.33 (m,<br>2H), 2.17–2.19 (m, 1H),<br>1.97–2.07 (m, 3H). |
| 78 |  | C | 770.6 | <sup>1</sup> H NMR (400 MHz, DMSO-<br>d <sub>6</sub> ): δ 11.08 (s, 1H), 9.35 (s,<br>1H), 8.64 (t, <i>J</i> = 3.9 Hz, 1H),<br>8.49 (d, <i>J</i> = 4.7 Hz, 1H), 8.32<br>(d, <i>J</i> = 8.1 Hz, 1H), 8.19 (dd,<br><i>J</i> = 8.6, 2.5 Hz, 1H), 7.98 (s,<br>1H), 7.68–7.48 (m, 3H), 7.31<br>(d, <i>J</i> = 7.8 Hz, 1H), 7.20 (t, <i>J</i><br>= 9.5 Hz, 1H), 6.94 (d, <i>J</i> =<br>8.6 Hz, 1H), 5.07 (dd, <i>J</i> =<br>12.9, 5.3 Hz, 1H), 4.33 (t, <i>J</i> =<br>6.5 Hz, 2H), 3.95 (s, 3H),<br>3.65 (m, 1H), 3.51–3.41 (m,<br>3H), 3.36–3.23 (m, 5H),<br>2.95–2.83 (m, 1H), 2.43–<br>2.28 (m, 6H), 2.05–1.96 (m,<br>1H), 1.79–1.73 (m, 1H).                                                             |

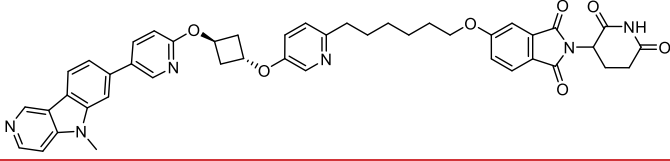
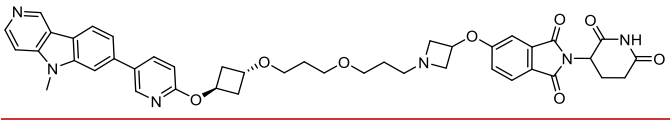
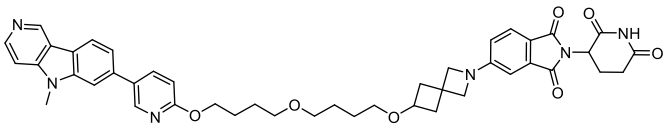
|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|----|-------------------------------------------------------------------------------------|---|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                     |   |       | 1.67–1.61 (m, 1H), 1.42 (m, 7H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| 79 |    | A | 759.6 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 9.35 (s, 1H), 8.59 (d, <i>J</i> = 5.7 Hz, 1H), 8.49 (s, 1H), 8.28 (s, 1H), 8.21 (d, <i>J</i> = 10.6 Hz, 1H), 8.00 (s, 1H), 7.91 (d, <i>J</i> = 11.0 Hz, 1H), 7.63 (d, <i>J</i> = 8.2 Hz, 1H), 7.57 (s, 1H), 7.51 (d, <i>J</i> = 9.3 Hz, 1H), 7.37 (d, <i>J</i> = 5.9 Hz, 1H), 6.85 (d, <i>J</i> = 8.6 Hz, 1H), 6.77 (s, 1H), 4.92 (m, 1H), 4.45 (s, 1H), 4.36 (t, <i>J</i> = 6.6 Hz, 2H), 4.16–4.26 (m, 2H), 3.83–3.98 (m, 4H), 3.44 (m, 4H), 2.63–2.92 (m, 3H), 2.11 (d, <i>J</i> = 6.4 Hz, 2H), 1.79–1.89 (m, 3H), 1.44–1.70 (m, 10H).                                                       |
| 80 |  | A | 759.6 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 11.12 (s, 1H), 9.35 (s, 1H), 8.63 (d, <i>J</i> = 2.3 Hz, 1H), 8.50 (s, 1H), 8.31 (d, <i>J</i> = 8.1 Hz, 1H), 8.18 (dd, <i>J</i> = 8.6, 2.5 Hz, 1H), 7.96 (s, 1H), 7.80 (d, <i>J</i> = 8.8 Hz, 1H), 7.60 (d, <i>J</i> = 6.8 Hz, 2H), 7.23 (d, <i>J</i> = 7.2 Hz, 2H), 6.93 (d, <i>J</i> = 8.6 Hz, 1H), 5.10 (m, 1H), 5.02 – 4.95 (m, 1H), 4.32 (t, <i>J</i> = 6.6 Hz, 2H), 3.95 (s, 3H), 3.70 (t, <i>J</i> = 6.8 Hz, 2H), 2.99 – 2.95 (m, 2H), 2.86 (d, <i>J</i> = 12.1 Hz, 2H), 2.64 (br, 1H), 2.55 (br, 2H), 2.33 (s, 2H), 2.06–1.96 (m, 3H), 1.81–1.70 (m, 3H), 1.60–1.40 (m, 8H). |
| 81 |  | A | 756.5 | <sup>1</sup> H NMR(400 MHz, CDCl <sub>3</sub> ): δ 9.31 (s, 1H), 8.51 (s, 1H), 8.40 (s, 1H), 8.11 (d, <i>J</i> = 8.0 Hz, 1H), 7.82–7.83 (m, 1H), 7.60 (s, 1H), 7.37–7.45 (m, 3H), 6.84 (d, <i>J</i> = 8.0 Hz, 1H), 4.92–4.95 (m, 1H), 4.53 (t, <i>J</i> = 4.8 Hz, 2H), 4.24 (t, <i>J</i> = 4.8 Hz, 2H), 3.89–3.91 (m, 4H), 3.67–3.75 (m, 12H), 2.74–2.92 (m, 3H), 2.12–2.16 (m, 1H).                                                                                                                                                                                                                                                               |
| 82 |  | C | 771.6 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 11.12 (s, 1H), 9.36 (s, 1H), 8.64 (d, <i>J</i> = 2.2 Hz, 1H), 8.50 (d, <i>J</i> = 5.7 Hz, 1H), 8.32 (d, <i>J</i> = 8.2 Hz, 1H), 8.19 (dd, <i>J</i> = 8.8, 2.6 Hz, 2H), 7.98 (s, 1H), 7.83 (d, <i>J</i> = 8.3 Hz, 1H), 7.62 (d, <i>J</i> = 8.4 Hz, 2H), 7.43 (d, <i>J</i> = 2.0 Hz, 1H), 7.35 (d, <i>J</i> = 8.4 Hz, 1H), 6.94 (d, <i>J</i> = 8.7 Hz, 1H), 5.31 (s, 1H), 5.12 (dd, <i>J</i> = 12.9, 5.3 Hz,                                                                                                                                                                           |

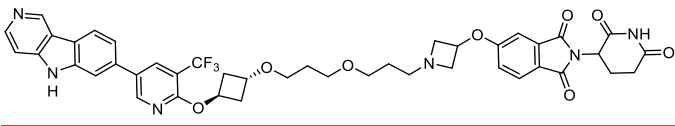
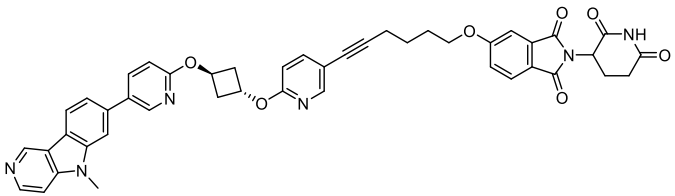
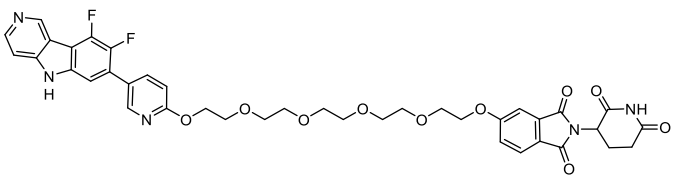
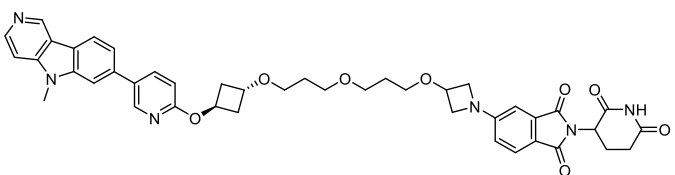
|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|----|-------------------------------------------------------------------------------------|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                     |   |       | 1H), 4.40 – 4.32 (m, 1H),<br>4.18 (t, <i>J</i> = 6.4 Hz, 2H), 3.96<br>(s, 3H), 2.88 (d, <i>J</i> = 13.2 Hz,<br>2H), 2.74 (s, 2H), 2.36 (m,<br>6H), 2.07 (s, 3H), 1.88 – 1.70<br>(m, 4H), 1.60 – 1.34 (m, 6H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 83 |    | C | 751.5 | <sup>1</sup> H NMR (400 MHz,<br>CD <sub>3</sub> OD): δ 9.58 (s,1H), 8.58<br>(d, <i>J</i> = 6.4 Hz, 1H), 8.54–<br>8.55 (d, <i>J</i> = 4 Hz, 1H), 8.47<br>(d, <i>J</i> = 8.4 Hz, 1H), 8.39 (d, <i>J</i><br>= 2.8 Hz, 1H), 8.12–8.17 (m,<br>2H), 7.97–8.01 (m, 2H), 7.91<br>(d, <i>J</i> = 9.2 Hz, 1H), 7.79–<br>7.83 (m, 2H), 7.39 (s, 1H),<br>7.32 (d, <i>J</i> = 8.0 Hz, 1H), 7.01<br>(d, <i>J</i> = 8.4 Hz, 1H), 5.50–<br>5.53 (m, 1H), 5.22–5.24 (m,<br>1H), 5.12–5.14 (m, 1H),<br>4.18–4.21 (m, 2H), 3.04–<br>3.07 (m, 2H), 2.74–2.84 (m,<br>7H), 2.18–2.20 (m, 1H),<br>2.09–2.13 (m, 1H), 2.02–<br>2.06 (m, 1H), 1.85–1.95 (m,<br>4H), 1.55–1.65 (m, 4H).                           |
| 84 |  | C | 794.5 | <sup>1</sup> H NMR(400 MHz, CDCl <sub>3</sub> ):<br>δ 9.34 (s, 1H), 8.58 (d, <i>J</i> =<br>5.6 Hz, 1H), 8.21-8.48 (m,<br>2H), 8.20 (d, <i>J</i> = 8.4 Hz, 1H),<br>7.88-7.91 (m, 1H), 7.76 (d, <i>J</i><br>= 8.4 Hz, 1H), 7.56 (s, 1H),<br>7.51 (d, <i>J</i> = 8.0 Hz, 1H),<br>7.33-7.36 (m, 2H), 7.16-7.18<br>(m, 2H), 6.86 (d, <i>J</i> = 8.4 Hz,<br>1H), 6.39-6.51 (m, 3H),<br>5.52-5.54 (m, 1H), 4.94-4.96<br>(m, 2H), 4.07-4.10 (m, 2H),<br>3.91-3.97 (m, 5H), 3.22-3.24<br>(m, 1H), 2.69-2.76 (m, 7H),<br>2.14-2.16 (m, 1H), 1.82-1.86<br>(m, 4H), 1.54-1.57 (m, 4H).                                                                                                              |
| 85 |  | A | 774.6 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ):<br>δ 9.32 (s, 1H), 8.58–8.59 (d,<br><i>J</i> = 4.0 Hz, 2H), 8.48 (s, 1H),<br>8.16–8.18 (d, <i>J</i> = 8.0 Hz,<br>1H), 7.89–7.91(d, <i>J</i> = 8.0 Hz,<br>1H), 7.74–7.76 (d, <i>J</i> = 8.0<br>Hz, 1H), 7.56 (s, 1H), 7.47–<br>7.49 (d, <i>J</i> = 8.0 Hz, 1H),<br>7.32–7.33 (d, <i>J</i> = 4.0 Hz,<br>1H), 7.19 (s, 1H), 7.06–7.08<br>(d, <i>J</i> = 8.0 Hz, 1H), 6.84–<br>6.86 (d, <i>J</i> = 8.0 Hz, 1H), 4.93<br>(m, 2H), 4.35–4.38 (m, 2H),<br>4.21 (s,1H), 3.90 (s, 3H),<br>3.35–3.49 (m, 7H), 2.68–<br>2.95 (m,3H), 2.44–2.51 (m,<br>4H), 2.15 (m, 1H), 1.88 (m,<br>2H), 1.56–1.68 (m, 9H), 1.44<br>(d, <i>J</i> = 8.0 Hz, 2H). |

|    |  |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|----|--|---|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 86 |  | C | 736.5 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ):<br>δ 9.28 (s, 2H), 8.50 (s, 1H),<br>8.08 (s, 1H), 7.35–7.57 (m,<br>6H), 6.94–6.96 (m, 3H),<br>6.77 (s, 1H), 6.38 (s, 1H),<br>4.88–4.90 (m, 1H), 4.14 (s,<br>2H), 3.60–3.86 (m, 17H),<br>3.31–3.34 (m, 2H), 2.66–<br>2.86 (m, 3H), 2.03–2.05 (m,<br>1H).                                                                                                                                                                                                                                                                                                                                                                                  |
| 87 |  | C | 739.5 | <sup>1</sup> H NMR(400 MHz, CDCl <sub>3</sub> ):<br>δ 9.28 (s, 1H), 8.42 (s, 1H),<br>8.37–8.39 (m, 2H), 8.06 (d, <i>J</i> =<br>8.0 Hz, 1H), 7.80 (d, <i>J</i> =<br>8.0 Hz, 1H), 7.62 (s, 1H),<br>7.40–7.45 (m, 3H), 6.09 (s,<br>1H), 6.82 (d, <i>J</i> = 8.8 Hz, 1H),<br>4.94–4.99 (m, 1H), 4.54 (t, <i>J</i> =<br>4.8 Hz, 4H), 3.86–3.91 (m,<br>4H), 3.66–3.75 (m, 12H),<br>2.73–2.92 (m, 3H), 2.20–<br>2.22 (m, 1H).                                                                                                                                                                                                                                                                     |
| 88 |  | A | 820.5 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ):<br>δ 9.35 (s, 1H), 8.63 (d, <i>J</i> = 7.6<br>Hz, 1H), 8.45 (s, 1H), 8.21<br>(d, <i>J</i> = 8.0 Hz, 1H), 8.16 (s,<br>1H), 7.87–7.90 (m, 1H), 7.75<br>(d, <i>J</i> = 8.4 Hz, 1H), 7.53–<br>7.58 (m, 2H), 7.39 (s, 1H),<br>7.35 (s, 1H), 7.21(d, <i>J</i> = 8.4<br>Hz, 1H), 6.91(d, <i>J</i> = 8.8 Hz,<br>1H), 4.87–4.92 (m, 3H), 4.55<br>(t, <i>J</i> = 4.8 Hz, 2H), 4.24 (t, <i>J</i> =<br>4.8 Hz, 2H), 3.90 (t, <i>J</i> = 4.4<br>Hz, 3H), 3.66–3.73 (m, 12<br>H), 2.76–2.87 (m, 3H), 2.09–<br>2.16 (m, 1H).                                                                                                                            |
| 89 |  | C | 841.6 | <sup>1</sup> H NMR: (400MHz, DMSO-<br>d <sub>6</sub> )<br>δ: 11.09 (s, 1H), 9.36 (s, 1H),<br>8.61 (d, <i>J</i> =2.4 Hz, 1H), 8.50<br>(d, <i>J</i> =5.6 Hz, 1H), 8.31 (d,<br><i>J</i> =8.0 Hz, 1H), 8.21 (s, 1H),<br>8.15 (dd, <i>J</i> =2.8, 8.8 Hz, 1H),<br>7.95 (s, 1H), 7.65 - 7.57 (m,<br>3H), 7.29 (s, 1H), 7.23 - 7.18<br>(m, 1H), 6.90 (d, <i>J</i> =8.8 Hz,<br>1H), 5.04 (dd, <i>J</i> =5.6, 12.8<br>Hz, 1H), 4.31 (t, <i>J</i> =6.4 Hz,<br>2H), 4.14 (br s, 1H), 4.10 -<br>3.99 (m, 3H), 3.96 (s, 3H),<br>3.87 (d, <i>J</i> =11.6 Hz, 2H), 3.74<br>(dd, <i>J</i> =5.6, 10.8 Hz, 2H),<br>3.02 - 2.81 (m, 4H), 1.98 -<br>1.86 (m, 2H), 1.85 - 1.72 (m,<br>4H), 1.63 - 1.15 (m, 9H). |

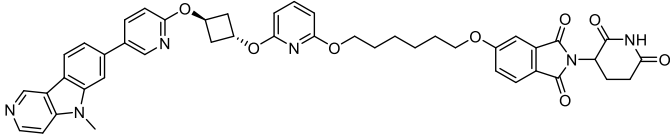
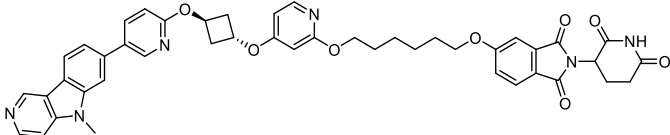
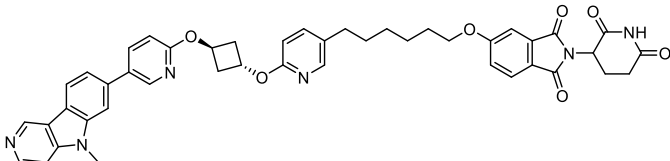
|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|----|-------------------------------------------------------------------------------------|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 90 |    | A | 744.5 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 9.35 (s, 1H), 8.60 (s, 1H), 8.50 (s, 1H), 8.20 (d, <i>J</i> = 8.0 Hz, 2H), 7.75 (d, <i>J</i> = 8.0 Hz, 1H), 7.55 (s, 1H), 7.49 (d, <i>J</i> = 8.0 Hz, 1H), 7.32 (d, <i>J</i> = 10.0 Hz, 2H), 7.16 (d, <i>J</i> = 8.0 Hz, 1H), 6.92 (d, <i>J</i> = 8.4 Hz, 1H), 5.10 (s, 2H), 4.98-5.00 (m, 1H), 4.21 (s, 2H), 4.07-4.10 (m, 2H), 3.90 (s, 3H), 3.44-3.54 (m, 7H), 2.76-2.87 (m, 3H), 2.18-2.23 (m, 2H), 1.88-1.92 (m, 3H), 1.72-1.75 (m, 4H).                                                                                                   |
| 91 |   | C | 798.6 | <sup>1</sup> H NMR(400 MHz, CD <sub>3</sub> OD): δ 9.33 (s, 1H), 8.51-8.53 (m, 2H), 8.33-8.34 (m, 1H), 8.09-8.11 (m, 1H), 7.84 (s, 1H), 7.59-7.62 (m, 3H), 7.30 (s, 1H), 7.17 (d, <i>J</i> = 8.4 Hz, 1H), 6.90 (d, <i>J</i> = 8.4 Hz, 1H), 5.32-5.35 (m, 1H), 3.99 (s, 3H), 3.40-3.47 (m, 13H), 2.69-2.71 (m, 6H), 2.50-2.52 (m, 4H), 2.03-2.18 (m, 5H), 1.59-1.60 (m, 6H).                                                                                                                                                                                                                         |
| 92 |  | A | 786.5 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 9.32 (s, 1H), 8.68 (s, 1H), 8.58 (s, 1H), 8.35 (s, 1H), 8.18 (d, <i>J</i> = 8.0 Hz, 1H), 7.97 (s, 1H), 7.74 (d, <i>J</i> = 8.4 Hz, 1H), 7.52 (s, 1H), 7.45 (d, <i>J</i> = 8.0 Hz, 1H), 7.27-7.34 (m, 2H), 7.20 (d, <i>J</i> = 7.6 Hz, 1H), 4.92-4.96 (m, 1H), 4.61 (s, 2H), 4.23 (s, 2H), 3.89-3.94 (m, 8H), 3.68-3.78 (m, 11H), 2.72-2.90 (m, 3H), 2.01-2.12 (m, 1H).                                                                                                                                                                          |
| 93 |  | C | 782.5 | <sup>1</sup> H NMR(400 MHz, CDCl <sub>3</sub> ): δ 9.35 (br, 1H), 8.94 (s, 1H), 8.59(s, 1H), 8.21 (d, <i>J</i> = 8.0 Hz, 1H), 8.01-8.09(m, 2H), 7.73 (d, <i>J</i> = 8.4 Hz, 1H), 7.69 (d, <i>J</i> = 8.0 Hz, 1H), 7.58 (s, 1H), 7.51(d, <i>J</i> = 8.4 Hz, 1H), 7.31(d, <i>J</i> = 5.2 Hz, 1H), 7.24(s, 1H), 7.09(dd, <i>J</i> = 8.0, 2.0 Hz, 1H), 4.85-4.90 (m, 1H), 4.10(t, <i>J</i> = 8.0 Hz, 1H), 3.98(t, <i>J</i> = 6.4 Hz, 1H), 3.87(s, 3H), 3.51 (t, <i>J</i> = 6.4 Hz, 1H), 3.27-3.32 (m, 4H), 2.65-2.85(m, 3H), 2.04-2.08 (m, 1H), 1.71-1.76 (m, 4H), 1.45-1.52 (m, 8H), 0.75-0.85(m, 4H). |

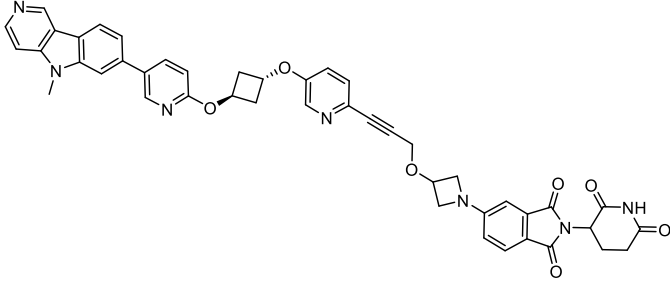
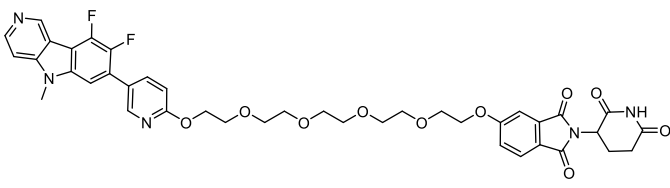
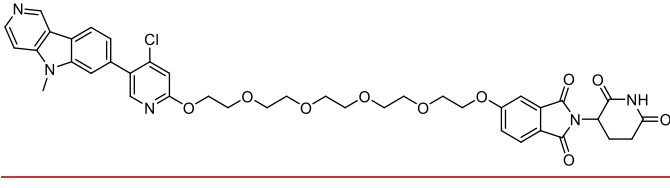
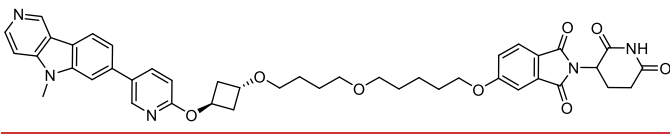
|           |                                                                                     |          |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-----------|-------------------------------------------------------------------------------------|----------|--------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <u>94</u> |    | <u>C</u> | <u>761.5</u> | <sup>1</sup> HNMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ: 11.04(s, 1H), 9.29(s, 1H), 8.58(d, <i>J</i> = 2.0 Hz, 1H), 8.43(d, <i>J</i> = 5.6 Hz, 1H), 8.25(d, <i>J</i> = 8.0 Hz, 1H), 8.12-8.16(m, 2H), 7.92(s, 1H), 7.78(d, <i>J</i> = 7.6 Hz, 1H), 7.56(d, <i>J</i> = 6.0 Hz, 2H), 7.40(s, 1H), 7.33(d, <i>J</i> = 8.4 Hz, 2H), 7.20-7.22(m, 1H), 6.92(d, <i>J</i> = 4.4 Hz, 1H), 5.37(s, 1H), 5.01-5.37(m, 2H), 4.25(t, <i>J</i> = 6.0 Hz, 2H), 3.89(s, 3H), 2.43-2.65(m, 9H), 1.98(t, <i>J</i> = 6.4 Hz, 3H).                                                                                                                                                                                                                                    |
| <u>95</u> |   | <u>C</u> | <u>765.5</u> | <sup>1</sup> HNMR (400 MHz, CDCl <sub>3</sub> ): δ: 9.32(s, 1H), 8.59(d, <i>J</i> = 4.8 Hz, 1H), 8.49(s, 1H), 8.20(d, <i>J</i> = 8.8 Hz, 1H), 8.16(s, 1H), 8.08(s, 1H), 7.94(d, <i>J</i> = 7.2 Hz, 1H), 7.77(d, <i>J</i> = 8.0 Hz, 1H), 7.56(s, 1H), 7.49(d, <i>J</i> = 8.4 Hz, 1H), 7.32(s, 2H), 7.17(d, <i>J</i> = 8.0 Hz, 1H), 7.07(s, 1H), 6.87(d, <i>J</i> = 8.8 Hz, 1H), 5.52(s, 1H), 4.94-4.97(m, 2H), 4.08(s, 2H), 3.91(s, 3H), 2.73-2.92(m, 8H), 2.13-2.15(m, 2H), 1.86-1.88(m, 2H), 1.78-1.80(m, 2H), 1.46-1.54(m, 2H).                                                                                                                                                                                                                       |
| <u>96</u> |  | <u>B</u> | <u>838.6</u> | <sup>1</sup> H NMR: 400 MHz, DMSO- <i>d</i> <sub>6</sub> δ : 11.09 (s, 1H), 9.38 (s, 1H), 8.64 (d, <i>J</i> =2.4 Hz, 1H), 8.51 (d, <i>J</i> =5.6 Hz, 1H), 8.33 (d, <i>J</i> =8.0 Hz, 1H), 8.19 (dd, <i>J</i> =2.4, 8.8 Hz, 1H), 8.14 (s, 1H), 7.99 (s, 1H), 7.72 - 7.59 (m, 3H), 7.21 (d, <i>J</i> =2.0 Hz, 1H), 7.12 (dd, <i>J</i> =2.0, 8.8 Hz, 1H), 6.94 (d, <i>J</i> =8.4 Hz, 1H), 5.38 - 5.26 (m, 1H), 5.06 (dd, <i>J</i> =5.3, 12.9 Hz, 1H), 4.24 - 4.13 (m, 1H), 3.96 (s, 3H), 3.95 - 3.88 (m, 1H), 3.72 (d, <i>J</i> =15.2 Hz, 1H), 3.68 - 3.63 (m, 1H), 3.53 (d, <i>J</i> =7.2 Hz, 1H), 3.31 (s, 2H), 3.07 - 2.75 (m, 4H), 2.74 - 2.54 (m, 4H), 2.44 - 2.29 (m, 4H), 2.06 - 1.94 (m, 1H), 1.50 (td, <i>J</i> =7.0, 13.8 Hz, 4H), 1.33 (s, 4H). |
| <u>97</u> |  | <u>B</u> | <u>775.5</u> | <sup>1</sup> H NMR(400 MHz, CDCl <sub>3</sub> ): δ 8.42-8.48 (m, 2H), 8.17-8.23 (m, 2H), 7.93 (d, <i>J</i> = 2 Hz, 1H), 7.75 (d, <i>J</i> = 8.4 Hz, 1H), 7.51-7.58 (m, 1H), 7.34 (s, 1H), 7.26-7.28 (m, 1H), 7.19 (d, <i>J</i> = 1.6 Hz, 1H), 7.05-7.17 (m, 1H), 6.87 (d, <i>J</i> = 8.4 Hz, 1H), 5.52-5.54 (m, 1H), 4.96-4.98 (m, 2H).                                                                                                                                                                                                                                                                                                                                                                                                                 |

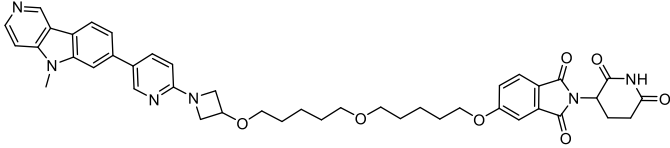
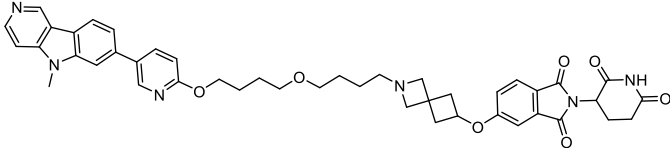
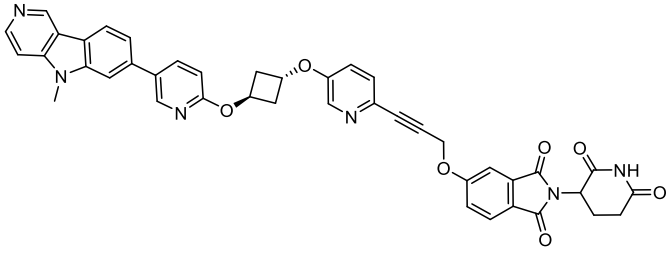
|            |                                                                                                  |          |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|------------|--------------------------------------------------------------------------------------------------|----------|--------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|            |                                                                                                  |          |              | 4.14-4.17 (m, 2H), 3.91 (s, 3H), 2.73-2.88 (m, 8H), 2.52-2.55 (m, 2H), 2.02-2.15 (m, 3H), 1.81-1.85 (m, 2H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <u>98</u>  | <div>  </div>   | <u>B</u> | <u>779.5</u> | <sup>1</sup> H NMR(400 MHz, CDCl <sub>3</sub> ): δ 8.48 (s, 1H), 8.26 (d, <i>J</i> = 7.6 Hz, 1H), 8.17 (s, 1H), 7.94 (d, <i>J</i> = 8.4 Hz, 1H), 7.75 (d, <i>J</i> = 8.4 Hz, 1H), 7.57-7.63 (m, 2H), 7.28-7.34 (m, 1H), 7.17-7.20 (m, 1H), 7.06 (s, 1H), 6.90 (d, <i>J</i> = 8.4 Hz, 1H), 5.53-5.55 (m, 1H), 4.97-5.01 (m, 2H), 4.06-4.16 (m, 2H), 3.98 (s, 3H), 2.71-2.88 (m, 8H), 2.51-2.53 (m, 1H), 2.02-2.21 (m, 4H), 1.62-1.85 (m, 4H), 1.51-1.56 (m, 4H), 0.82-0.92 (m, 2H).                                                                                                                                                                                                                                                     |
| <u>99</u>  | <div>  </div> | <u>A</u> | <u>773.5</u> | <sup>1</sup> H NMR (400 Hz, DMSO-d <sub>6</sub> ): δ 1.40-1.56 (m, 2H), 1.62-1.75 (m, 2H), 1.83-2.09 (m, 2H), 2.34-2.50 (m, 3H), 2.58-2.73 (m, 2H), 2.83-2.93 (m, 1H), 3.01-3.13 (m, 2H), 3.37-3.52 (m, 8H), 3.77 (s, 2H), 3.95 (s, 3H), 4.18 (s, 1H), 5.02-5.13 (m, 2H), 5.29-5.37 (m, 1H), 6.94 (d, <i>J</i> = 8.0 Hz, 1H), 7.21-7.29 (m, 2H), 7.59-7.65 (m, 2H), 7.80 (d, <i>J</i> = 7.2 Hz, 1H), 7.97 (s, 1H), 8.18 (d, <i>J</i> = 7.6 Hz, 1H), 8.31 (d, <i>J</i> = 7.6 Hz, 1H), 8.50 (d, <i>J</i> = 5.2 Hz, 1H), 8.63 (s, 1H), 9.35 (s, 1H), 11.11 (s, 1H).                                                                                                                                                                       |
| <u>100</u> | <div>  </div> | <u>C</u> | <u>771.6</u> | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 1.65-1.67 (m, 6H), 1.74-1.81 (m, 2H), 1.87-1.94 (m, 2H), 2.00-2.06 (m, 1H), 2.09-2.14 (m, 1H), 2.18-2.24 (m, 2H), 2.54-2.59 (m, 2H), 2.68-2.90 (m, 3H), 3.37-3.53 (m, 5H), 3.91 (t, <i>J</i> = 7.6 Hz, 3H), 3.98 (d, <i>J</i> = 8.0 Hz, 3H), 4.39 (t, <i>J</i> = 6.4 Hz, 2H), 4.90-4.94 (m, 1H), 6.45 (d, <i>J</i> = 1.6 Hz, 1H), 6.72 (d, <i>J</i> = 1.6 Hz, 1H), 6.85 (d, <i>J</i> = 8.4 Hz, 1H), 7.35 (d, <i>J</i> = 6 Hz, 1H), 7.50 (d, <i>J</i> = 8.0 Hz, 1H), 7.56 (s, 1H), 7.61 (d, <i>J</i> = 8.0 Hz, 1H), 7.91 (d, <i>J</i> = 2.4 Hz, 1H), 8.05 (s, 1H), 8.21 (d, <i>J</i> = 8.0 Hz, 1H), 8.49 (d, <i>J</i> = 2.4 Hz, 1H), 8.60 (d, <i>J</i> = 5.6 Hz, 1H), 9.34 (s, 1H). |

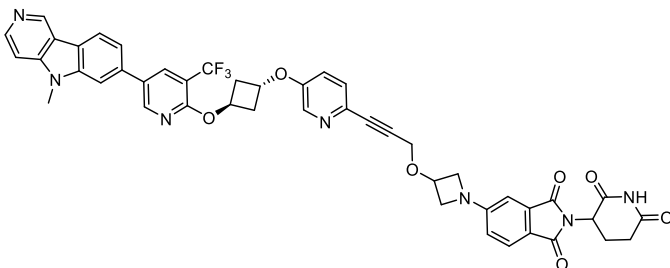
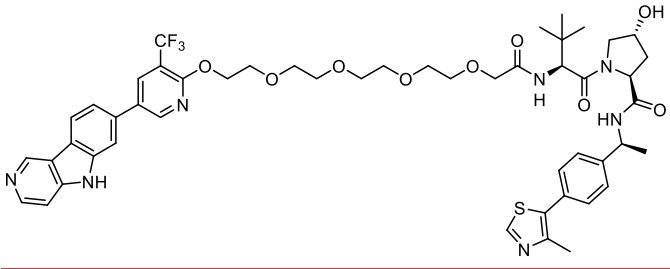
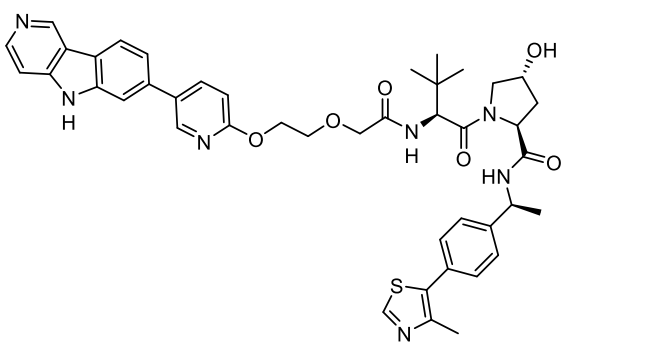
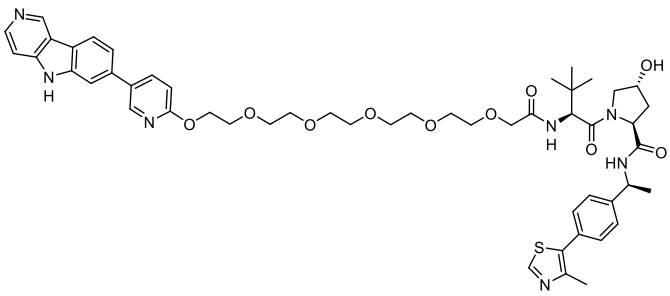
|     |                                                                                     |    |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-----|-------------------------------------------------------------------------------------|----|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 101 |    | A  | 827.5 | <p><sup>1</sup>H NMR (400 Hz, D6-DMSO): δ 1.56-1.59 (m, 2H), 1.71-1.77 (m, 2H), 1.95-2.05 (m, 2H), 2.34-2.46 (m, 3H), 2.50-2.67 (m, 3H), 2.83-2.93 (m, 1H), 3.32-3.49 (m, 9H), 3.88-3.92 (m, 1H), 4.17-4.20 (m, 1H), 4.55 (t, <i>J</i> = 5.6 Hz, 1H), 5.05-5.13 (m, 2H), 5.46-5.49 (m, 1H), 7.25-7.28 (m, 2H), 7.52 (d, <i>J</i> = 5.6 Hz, 1H), 7.63 (d, <i>J</i> = 8.0 Hz, 1H), 7.82 (d, <i>J</i> = 8.0 Hz, 1H), 7.87 (s, 1H), 8.33 (d, <i>J</i> = 8.0 Hz, 1H), 8.39 (s, 1H), 8.45 (d, <i>J</i> = 6.0 Hz, 1H), 8.83 (s, 1H), 9.39 (s, 1H), 11.11 (s, 1H), 11.86 (s, 1H).</p>                                           |
| 102 |  | C  | 775.5 | <p><sup>1</sup>HNMR (400 MHz, DMSO-<i>d</i><sub>6</sub>): δ 1.73 (d, <i>J</i> = 7.2 Hz, 2H), 1.91 (d, <i>J</i> = 7.2 Hz, 2H), 2.01-2.08 (m, 1H), 2.51-2.67 (m, 8H), 2.83-2.94 (m, 1H), 3.96 (s, 3H), 4.24 (t, <i>J</i> = 6.0 Hz, 2H), 5.12 (dd, <i>J</i> = 12.8, 5.2 Hz, 1H), 5.31-5.52 (m, 2H), 6.99 (d, <i>J</i> = 8.4 Hz, 1H), 6.83 (d, <i>J</i> = 8.6 Hz, 1H), 7.36 (d, <i>J</i> = 8.2 Hz, 1H), 7.44 (s, 1H), 7.75-7.58 (m, 3H), 7.82 (d, <i>J</i> = 8.2 Hz, 1H), 7.99 (s, 1H), 8.10-8.28 (m, 2H), 8.33 (d, <i>J</i> = 8.2 Hz, 1H), 8.52 (s, 1H), 8.64 (d, <i>J</i> = 1.6 Hz, 1H), 9.40 (s, 1H), 11.11 (s, 1H).</p> |
| 103 |  | ND | 774.5 | <p><sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ 9.46 (s, 1H), 8.63 (d, <i>J</i> = 6.8 Hz, 1H), 8.38 (s, 1H), 8.00 (d, <i>J</i> = 6.8 Hz, 1H), 7.96 (d, <i>J</i> = 8.8 Hz, 1H), 7.67 (d, <i>J</i> = 8.4 Hz, 1H), 7.61 (d, <i>J</i> = 4.8 Hz, 1H), 7.29 (s, 1H), 7.23 (d, <i>J</i> = 8.4 Hz, 1H), 6.93 (d, <i>J</i> = 8.8 Hz, 1H), 5.05 (m, 1H), 4.54 – 4.45 (m, 2H), 4.26 – 4.19 (m, 2H), 3.86 (m, 4H), 3.70-3.65 (m, 12H), 2.86 – 2.62 (m, 3H), 2.10 – 2.04 (m, 1H).</p>                                                                                                                                            |
| 104 |  | A  | 773.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-<i>d</i><sub>6</sub>): δ 1.73-1.79 (m, 4H), 1.97-1.99 (m, 2H), 2.31-2.37 (m, 2H), 2.40-2.49 (m, 2H), 2.54-2.59 (m, 1H), 2.83-2.88 (m, 1H), 3.38 (t, <i>J</i> = 6.4 Hz, 2H), 3.43-3.49 (m, 6H), 3.82-3.85 (m, 2H), 3.75 (s, 3H), 4.16-4.18 (m, 1H), 4.20-4.26 (m, 2H), 4.43-4.47 (m, 1H), 5.02-5.07 (m, 1H), 5.31-5.34 (m, 1H), 6.62-6.64 (m, 1H), 6.78-6.79 (m, 1H).</p>                                                                                                                                                                                                            |

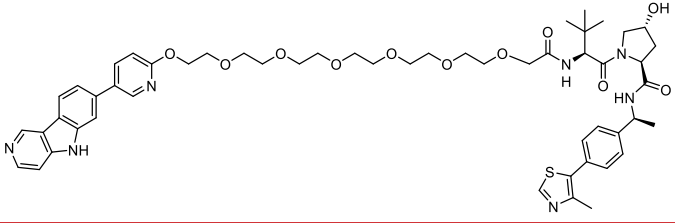
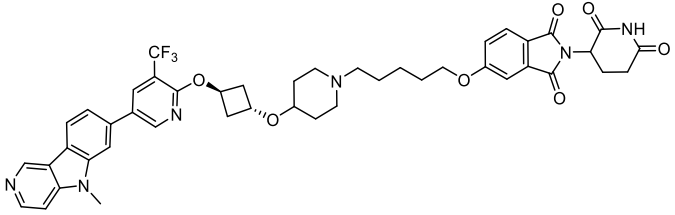
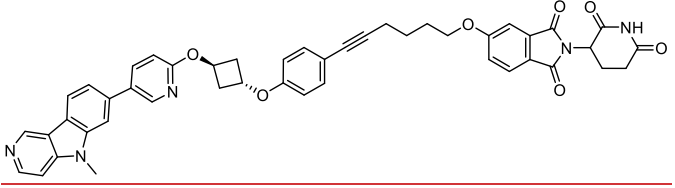


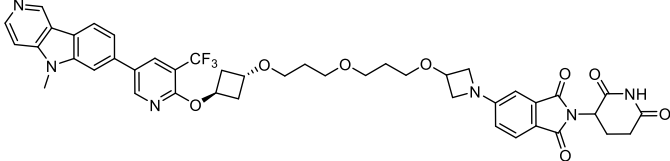
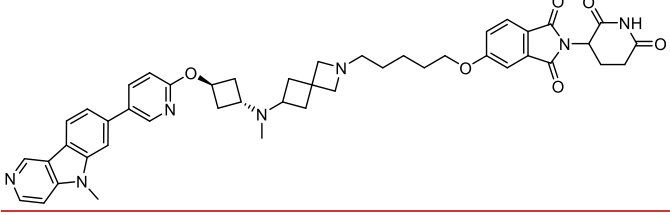
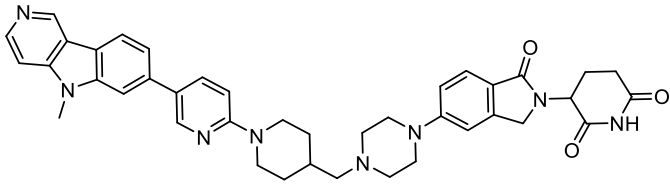
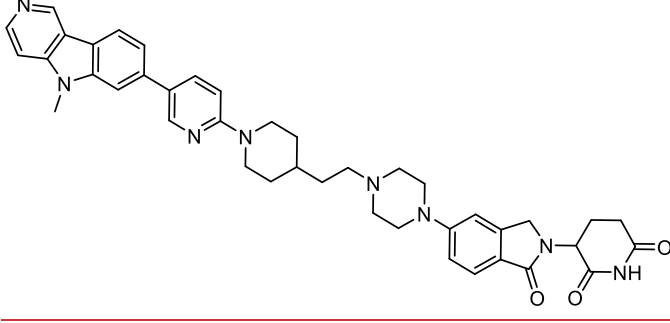
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----|-------------------------------------------------------------------------------------|---|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 108 |    | C | 795.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.43-1.44 (m, 4H), 1.70-1.74 (m, 4H), 1.98-2.04 (m, 1H), 2.44-2.47 (m, 1H), 2.56-2.60 (m, 1H), 2.65 (t, <i>J</i> = 6.0 Hz, 4H), 2.83-2.92 (m, 1H), 3.95 (s, 3H), 4.10 (t, <i>J</i> = 6.0 Hz, 2H), 4.22 (t, <i>J</i> = 6.4 Hz, 2H), 5.07-5.11 (m, 1H), 5.30-5.35 (m, 1H), 5.39-5.45 (m, 1H), 6.34-6.37 (m, 2H), 6.98 (d, <i>J</i> = 8.4 Hz, 1H), 7.24-7.26 (m, 1H), 7.33 (d, <i>J</i> = 2.0 Hz, 1H), 7.59-7.65 (m, 3H), 7.72 (d, <i>J</i> = 8.0 Hz, 1H), 7.97 (s, 1H), 8.17-8.21 (m, 1H), 8.31 (d, <i>J</i> = 8.0 Hz, 1H), 8.50 (d, <i>J</i> = 6.0 Hz, 1H), 8.65 (d, <i>J</i> = 2.0 Hz, 1H), 9.36 (s, 1H), 11.10 (s, 1H).                             |
| 109 |  | C | 795.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.47 (s, 4H), 1.72-1.78 (m, 4H), 2.02-2.05 (m, 2H), 2.33 (s, 1H), 2.63-2.66 (m, 4H), 2.88-2.89 (m, 1H), 3.41-3.49 (m, 2H), 3.96 (s, 2H), 4.18-4.23 (m, 3H), 5.04-5.12 (m, 2H), 5.42 (br, 1H), 6.19 (s, 1H), 6.55-6.56 (m, 1H), 6.98 (d, <i>J</i> = 8.4 Hz, 1H), 7.34 (d, <i>J</i> = 7.2 Hz, 1H), 7.41 (s, 1H), 6.63 (s, 2H), 7.81-7.83 (m, 1H), 7.95-7.97 (m, 2H), 8.21 (d, <i>J</i> = 8.4 Hz, 1H), 8.32 (d, <i>J</i> = 7.2 Hz, 1H), 8.50 (d, <i>J</i> = 4.0 Hz, 1H), 8.64 (s, 1H), 9.36 (s, 1H), 11.11 (s, 1H).                                                                                                                                     |
| 110 |  | C | 779.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.36 (d, <i>J</i> = 7.6 Hz, 2H), 1.45 (d, <i>J</i> = 6.8 Hz, 2H), 1.52-1.61 (m, 2H), 1.70-1.80 (m, 2H), 1.98-2.02 (m, 3H), 2.54-2.70 (m, 6H), 2.89 (t, <i>J</i> = 16.6 Hz, 1H), 3.96 (s, 3H), 4.16 (d, <i>J</i> = 5.0 Hz, 2H), 5.12 (dd, <i>J</i> = 12.8, 4.4 Hz, 1H), 5.36-5.43 (m, 2H), 6.77 (d, <i>J</i> = 8.4 Hz, 1H), 6.99 (d, <i>J</i> = 8.0 Hz, 1H), 7.34 (d, <i>J</i> = 8.8 Hz, 1H), 7.42 (s, 1H), 7.60-7.64 (m, 3H), 7.83 (d, <i>J</i> = 8.0 Hz, 1H), 7.97 (dd, <i>J</i> = 14.0, 6.4 Hz, 2H), 8.33 (d, <i>J</i> = 8.4 Hz, 1H), 8.21 (d, <i>J</i> = 8.0 Hz, 1H), 8.50 (d, <i>J</i> = 4.8 Hz, 1H), 8.65 (s, 1H), 9.37 (s, 1H), 11.11 (s, 1H). |

|     |                                                                                     |   |                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-----|-------------------------------------------------------------------------------------|---|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 111 |    | C | 788.5            | <sup>1</sup> HNMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.98-2.02 (m, 1H), 2.54-2.73 (m, 6H), 2.83-2.92 (m, 1H), 3.95-3.97 (m, 5H), 4.31-4.34 (m, 2H), 4.50 (s, 2H), 4.67-4.72 (m, 1H), 5.04-5.13 (m, 2H), 5.42-5.48 (m, 1H), 6.67-6.69 (m, 1H), 6.82 (s, 1H), 6.69-7.01 (m, 1H), 7.33-7.36 (m, 1H), 7.53-7.55 (m, 1H), 7.63-7.67 (m, 3H), 8.01 (s, 1H), 8.21-8.26 (m, 2H), 8.33-8.37 (m, 1H), 8.51-8.55 (m, 1H), 8.65-8.66 (m, 1H), 9.39 (s, 1H), 11.07 (s, 1H).                                                                                                      |
| 112 |   | A | 788.5            | <sup>1</sup> HNMR (400 MHz, CDCl <sub>3</sub> ): δ: 11.09(s, 1H), 9.25(s, 1H), 8.50(s, 1H), 8.59(s, 1H), 8.07(d, <i>J</i> = 8.4 Hz, 1H), 7.79(d, <i>J</i> = 8.4 Hz, 1H), 7.69-7.73(m, 2H), 7.75(d, <i>J</i> = 8.4 Hz, 1H), 7.42(s, 1H), 7.34(d, <i>J</i> = 8.4 Hz, 1H), 7.02(d, <i>J</i> = 8.4 Hz, 1H), 5.08-5.13(m, 1H), 4.46(d, <i>J</i> = 4.4 Hz, 2H), 4.30-4.34(m, 2H), 3.95(s, 3H), 3.79(s, 4H), 3.60(s, 4H), 3.56(s, 4H), 3.53(s, 4H), 2.85-2.88(m, 1H), 2.61(s, 2H).                                                                                         |
| 113 |  | C | 786.5<br>[788.5] | <sup>1</sup> HNMR (400 MHz, DMSO-d <sub>6</sub> ): δ 11.11 (s, 1H), 9.35 (s, 1H), 8.50 (s, 1H), 8.38 (s, 1H), 8.29 (d, <i>J</i> = 8.0 Hz, 1H), 7.87 (s, 1H), 7.75 (d, <i>J</i> = 8.0 Hz, 1H), 7.62 (d, <i>J</i> = 5.6 Hz, 1H), 7.52 (d, <i>J</i> = 8.0 Hz, 1H), 7.34 (d, <i>J</i> = 8.4 Hz, 2H), 7.27 (d, <i>J</i> = 10.4 Hz, 1H), 5.13-5.08 (m, 1H), 4.34-4.32 (m, 2H), 4.23-4.21 (m, 2H), 3.91 (s, 3H), 3.77-3.71 (m, 4H), 3.54-3.46 (m, 12 H), 2.91-2.87 (m, 1H), 2.61-2.57 (m, 3H).                                                                             |
| 114 |  | C | 760.5            | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 1.52-1.59 (m, 2H), 1.63-1.67 (m, 5H), 1.83-1.90 (m, 1H), 2.11-2.16 (m, 2H), 2.43-2.54 (m, 4H), 2.71-2.92 (m, 4H), 3.39-3.49 (m, 6H), 3.95 (s, 3H), 4.08 (t, <i>J</i> = 6.4 Hz, 2H), 4.23-4.29 (m, 1H), 4.94 (dd, <i>J</i> = 5.2, 12.0 Hz, 1H), 6.83 (d, <i>J</i> = 8.4 Hz, 1H), 7.17 (dd, <i>J</i> = 2.0, 8.0 Hz, 1H), 7.32 (d, <i>J</i> = 1.6 Hz, 1H), 7.44 (d, <i>J</i> = 6.0 Hz, 1H), 7.54 (d, <i>J</i> = 8.0 Hz, 1H), 7.60 (s, 1H), 7.75 (d, <i>J</i> = 8.4 Hz, 1H), 7.91 (dd, <i>J</i> = 2.4, 8.8 Hz, 1H). |

|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----|-------------------------------------------------------------------------------------|---|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | <p>8.14 (m, 1H), 8.21 (d, <math>J</math> = 8.0 Hz, 1H), 8.48 (d, <math>J</math> = 2.4 Hz, 1H), 8.58 (d, <math>J</math> = 5.2 Hz, 1H), 9.34 (s, 1H).</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| 115 |    | C | 759.6 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.34-1.38 (m, 2H), 1.40-1.58 (m, 8H), 1.74-1.77 (m, 2H), 2.01-2.04 (m, 1H), 2.54-2.61 (m, 1H), 2.84-2.93 (m, 1H), 3.32-3.42 (m, 7H), 3.77-3.81 (m, 2H), 3.96 (s, 3H), 4.15 (t, <math>J</math> = 6.4 Hz, 2H), 4.21 (t, <math>J</math> = 8.8 Hz, 2H), 4.40-4.45 (m, 1H), 5.10 (dd, <math>J</math> = 12.8 Hz, 1H), 6.52 (d, <math>J</math> = 8.8 Hz, 1H), 7.32 (dd, <math>J</math> = 8.0 Hz, 1H), 7.39 (s, 1H), 7.58 (d, <math>J</math> = 8.0 Hz, 1H), 7.65 (d, <math>J</math> = 6.0 Hz, 1H), 7.80 (d, <math>J</math> = 8.4 Hz, 1H), 7.91 (s, 1H), 8.01 (dd, <math>J</math> = 8.4 Hz, 1H), 8.29 (d, <math>J</math> = 8.0 Hz, 1H), 8.50 (d, <math>J</math> = 5.6 Hz, 1H), 8.58 (s, 1H), 9.36 (s, 1H), 11.10 (s, 1H).</p> |
| 116 |  | C | 771.6 | <p><sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 1.39-1.42 (m, 2H), 1.47-1.52 (m, 2H), 1.64-1.70 (m, 2H), 1.77-1.82 (m, 2H), 2.01-2.07 (m, 1H), 2.21-2.26 (m, 2H), 2.54-2.64 (m, 3H), 2.75-2.90 (m, 5H), 3.42-3.45 (m, 3H), 3.61-3.71 (m, 4H), 3.95 (s, 3H), 4.35 (t, <math>J</math> = 6.2 Hz, 2H), 4.78-4.82 (m, 1H), 5.09-5.13 (m, 1H), 6.94 (d, <math>J</math> = 8.4 Hz, 1H), 7.20-7.25 (m, 2H), 7.60-7.63 (m, 2H), 7.79 (d, <math>J</math> = 8.0 Hz, 1H), 7.97 (s, 1H), 8.18-8.20 (m, 1H), 8.31 (d, <math>J</math> = 8.0 Hz, 1H), 8.48 (d, <math>J</math> = 5.2 Hz, 1H), 8.65 (s, 1H), 9.34 (s, 1H), 11.11 (s, 1H).</p>                                                                                                                                             |
| 117 |  | C | 733.4 | <p><sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ 1.92-1.94 (m, 1H), 2.02-2.10 (m, 2H), 2.62-2.65 (m, 5H), 3.90 (s, 3H), 4.97-5.02 (m, 2H), 5.10 (s, 2H), 5.37 (t, <math>J</math> = 6 Hz, 1H), 6.85 (d, <math>J</math> = 8.4 Hz, 1H), 7.20-7.22 (m, 1H), 7.34-7.41 (m, 2H), 7.45 (d, <math>J</math> = 2.0 Hz, 1H), 7.50-7.56 (m, 2H), 7.75-7.77 (m, 2H), 8.02-8.06 (m, 2H), 8.21 (d, <math>J</math> = 8.0 Hz, 1H), 8.37 (d, <math>J</math> = 6.0 Hz, 1H), 8.42 (d, <math>J</math> = 2.4 Hz, 1H), 9.18 (s, 1H).</p>                                                                                                                                                                                                                                                       |

|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-----|-------------------------------------------------------------------------------------|---|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 118 |    | C | 856.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.98-2.03 (m, 1H), 2.09-2.15 (m, 1H), 2.20-2.24 (m, 1H), 2.70-2.87 (m, 5H), 4.01-4.04 (m, 4H), 4.29-4.34 (m, 1H), 4.46 (s, 2H), 4.75-4.79 (m, 1H), 4.89-4.95 (m, 1H), 5.00-5.06 (m, 1H), 5.33-5.40 (m, 2H), 5.65-5.70 (m, 1H), 6.53-6.55 (m, 1H), 6.79 (s, 1H), 7.08-7.11 (m, 1H), 7.40 (d, <i>J</i> = 8.0 Hz, 1H), 7.56-7.65 (m, 4H), 7.95 (s, 1H), 8.19-8.30 (m, 3H), 8.60-8.64 (m, 2H), 9.38 (s, 1H).                                                                                                               |
| 119 |   | C | 990.7 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 0.93 (s, 9H), 1.35 (t, <i>J</i> = 6.8 Hz, 3H), 1.77-1.78 (s, 1H), 2.02-2.04 (m, 1H), 2.44 (s, 3H), 3.53-3.64 (m, 14H), 3.80-3.85 (m, 2H), 3.95 (s, 2H), 4.28 (s, 1H), 4.44 (d, <i>J</i> = 8.2 Hz, 1H), 4.54 (d, <i>J</i> = 9.6 Hz, 1H), 4.58-4.63 (m, 2H), 4.90 (s, 1H), 5.12 (s, 1H), 7.26-7.50 (m, 5H), 7.54 (d, <i>J</i> = 5.8 Hz, 1H), 7.66 (d, <i>J</i> = 8.2 Hz, 1H), 7.90 (s, 1H), 8.35 (d, <i>J</i> = 8.0 Hz, 1H), 8.42-8.45 (m, 3H), 8.85 (s, 1H), 8.97 (s, 1H), 9.41 (s, 1H), 11.92 (s, 1H).                 |
| 120 |  | C | 790.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 0.95 (s, 9H), 1.37-1.47 (m, 3H), 1.75-1.81 (m, 1H), 2.03-2.08 (m, 1H), 2.44 (s, 3H), 3.16-3.17 (m, 4H), 3.29 (s, 2H), 3.54-3.63 (m, 2H), 3.89 (s, 2H), 4.06 (s, 3H), 4.26-4.31 (m, 1H), 4.44-4.51 (m, 3H), 4.56-4.61 (m, 1H), 4.90-4.96 (m, 1H), 5.10-5.17 (m, 1H), 7.06-7.10 (m, 1H), 7.36-7.38 (m, 2H), 7.42-7.48 (m, 3H), 7.53-7.56 (m, 1H), 7.57-7.61 (m, 1H), 7.80 (s, 1H), 8.10-8.14 (m, 1H), 8.32 (s, 1H), 8.44-8.46 (m, 2H), 8.58 (d, <i>J</i> = 2.0 Hz, 1H), 8.97 (s, 1H), 9.40 (s, 1H), 11.90-11.98 (m, 1H). |
| 121 |  | B | 966.7 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 0.93 (s, 9H), 1.36-1.47 (m, 3H), 1.73-1.80 (m, 1H), 1.96-2.09 (m, 2H), 3.23-3.60 (m, 16H), 3.79 (t, <i>J</i> = 3.6 Hz, 2H), 3.96 (s, 2H), 4.28 (s, 1H), 4.42-4.46 (m, 3H), 4.54 (d, <i>J</i> = 9.6 Hz, 1H), 4.90 (t, <i>J</i> = 7.6 Hz, 1H), 5.12 (s, 1H), 6.97 (d, <i>J</i> = 8.4 Hz,                                                                                                                                                                                                                                 |

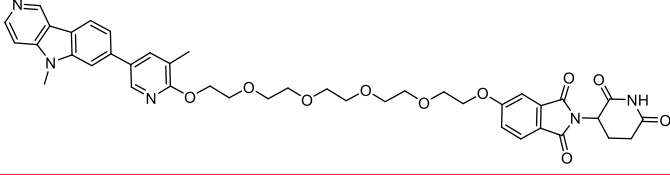
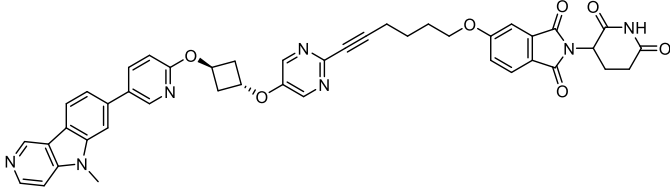
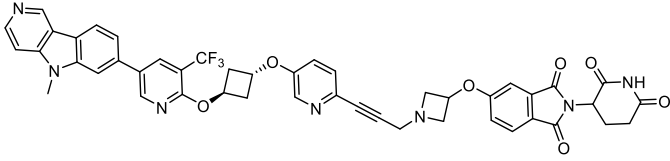
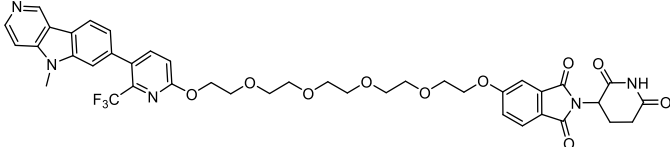
|     |                                                                                     |   |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|-----|-------------------------------------------------------------------------------------|---|--------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |        | 1H), 7.35-7.43 (m, 5H),<br>7.65-7.69 (m, 2H), 7.87 (s,<br>1H), 8.12-8.15 (m, 1H),<br>8.37-8.43 (m, 2H), 8.51 (d, <i>J</i><br>= 5.6 Hz, 1H), 8.59 (d, <i>J</i> =<br>1.6 Hz, 1H), 8.97 (s, 1H),<br>9.51 (s, 1H), 12.28 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| 122 |    | C | 1010.7 | <sup>1</sup> H NMR (400 MHz,<br>DMSO-d <sub>6</sub> ): δ 0.93 (s, 9H),<br>1.36 (d, <i>J</i> = 7.2 Hz, 3H),<br>1.73-1.80 (m, 1H), 2.01-2.05<br>(m, 1H), 2.44 (s, 1H), 3.51-<br>3.60 (m, 20H), 3.78 (t, <i>J</i> =<br>4.4 Hz, 2H), 3.95 (s, 2H),<br>4.06-4.10 (m, 1H), 4.27 (s,<br>1H), 4.42-4.46 (m, 3H), 4.54<br>(d, <i>J</i> = 9.6 Hz, 1H), 4.90 (t, <i>J</i><br>= 7.2 Hz, 1H), 5.12 (d, <i>J</i> =<br>3.6 Hz, 1H), 6.97 (d, <i>J</i> = 8.8<br>Hz, 1H), 7.35-7.38 (m, 3H),<br>7.41-7.43 (m, 2H), 7.48 (d, <i>J</i><br>= 5.6 Hz, 1H), 7.56 (d, <i>J</i> = 8.0<br>Hz, 1H), 7.77 (s, 1H), 8.10-<br>8.13 (m, 1H), 8.30 (d, <i>J</i> = 8.0<br>Hz, 1H), 8.42 (d, <i>J</i> = 6.0 Hz,<br>2H), 8.56 (d, <i>J</i> = 2.4 Hz, 1H),<br>8.97 (s, 1H), 9.35 (s, 1H),<br>11.79 (s, 1H). |
| 123 |  | C | 839.6  | <sup>1</sup> HNMR (400 MHz, DMSO-<br>d <sub>6</sub> ): δ: 11.11(s, 1H),<br>9.39(s,1H), 8.91(s,1H),<br>8.51(s,1H), 8.36(d, <i>J</i> = 8.0<br>Hz, 1H), 8.19(s, 1H),<br>8.10(s,1H), 7.83(d, <i>J</i> = 8.4<br>Hz, 1H), 7.71(d, <i>J</i> = 8.4 Hz,<br>1H), 7.64(d, <i>J</i> = 5.2 Hz, 1H),<br>7.43(s, 1H), 7.34(d, <i>J</i> = 8.0<br>Hz, 1H), 5.42-5.47(m, 1H),<br>5.09-5.14(m, 1H), 4.36(s,<br>1H), 4.18(t, <i>J</i> = 6.4 Hz, 2H),<br>4.24(t, <i>J</i> = 4.8 Hz, 2H),<br>3.98(s, 3H), 2.80-2.91(m,<br>1H), 2.74-2.76(m, 2H), 2.40-<br>2.46(m, 4H), 2.32(t, <i>J</i> = 6.4<br>Hz, 2H), 2.05-2.07(m, 4H),<br>1.76-1.82(m, 4H), 1.44-<br>1.48(m, 4H).                                                                                                                         |
| 124 |  | C | 774.5  | <sup>1</sup> H NMR(400 MHz, CDCl <sub>3</sub> ):<br>δ 8.49 (s, 1H), 8.22 (m, <i>J</i> =<br>7.6 Hz, 1H), 8.17 (s, 1H),<br>7.94 (d, <i>J</i> = 2 Hz, 1H), 7.76<br>(d, <i>J</i> = 8.4 Hz, 1H), 7.59 (s,<br>1H), 7.52 (d, <i>J</i> = 7.6 Hz, 1H),<br>7.34 (d, <i>J</i> = 1.2 Hz, 1H),<br>7.30-7.27 (m, 4H), 7.20-7.18<br>(m, 1H), 6.87 (d, <i>J</i> = 8.8 Hz,<br>1H), 6.74 (d, <i>J</i> = 8.4 Hz, 2H),<br>5.52-5.54 (m, 1H), 4.97-4.94<br>(m, 2H), 4.16 (t, <i>J</i> = 6.0 Hz,<br>2H), 3.92 (s, 3H), 2.88-2.69<br>(m, 8H), 2.50 (t, <i>J</i> = 6.8 Hz,<br>2H), 2.16-2.13 (m, 2H).                                                                                                                                                                                            |

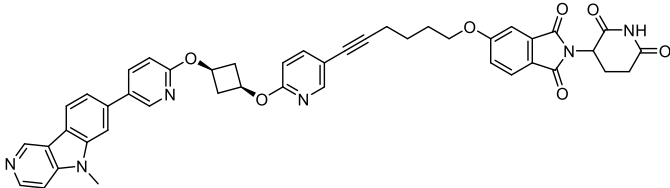
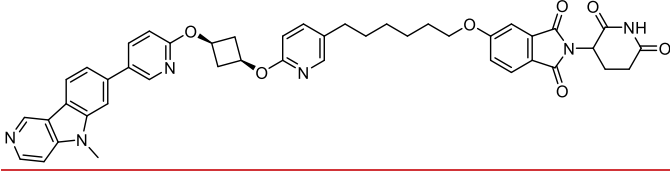
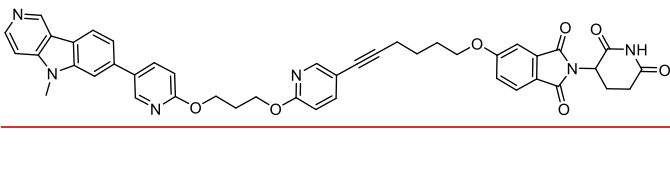
|                     |                                                                                                  |                   |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|---------------------|--------------------------------------------------------------------------------------------------|-------------------|-----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                     |                                                                                                  |                   |                       | <a href="#">1.82-1.78 (m, 2H).</a>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <a href="#">125</a> | <div>  </div>   | <a href="#">C</a> | <a href="#">841.5</a> | <a href="#">1H NMR (400 MHz, DMSO-d6): δ 1.85-1.90 (m, 4H), 2.08-2.19 (m, 2H), 2.20-2.26 (m, 2H), 2.44-2.57 (m, 4H), 2.70-2.90 (m, 3H), 3.45-3.49 (m, 2H), 3.53-3.56 (m, 6H), 3.88-3.91 (m, 2H), 4.22-4.29 (m, 3H), 4.47-4.48 (m, 1H), 4.90-4.94 (m, 1H), 5.53-5.55 (m, 1H), 6.51 (d, J = 8.0 Hz, 1H), 6.77 (s, 1H), 7.47 (d, J = 17.2 Hz, 2H), 7.58 (s, 1H), 7.60 (d, J = 8.4 Hz, 1H), 8.16 (s, 1H), 8.23-8.28 (m, 2H), 8.60 (s, 2H), 9.41 (s, 1H).</a>                                                                        |
| <a href="#">126</a> | <div>  </div> | <a href="#">B</a> | <a href="#">796.6</a> | <a href="#">1H NMR (400 MHz, DMSO-d6): δ 1.42-1.51 (m, 4H), 1.75-1.79 (m, 2H), 2.03-2.06 (m, 1H), 2.54 (s, 3H), 2.58-2.68 (m, 5H), 2.81-2.94 (m, 2H), 3.11-3.17 (m, 2H), 3.61-3.71 (m, 3H), 3.98-4.11 (m, 6H), 4.15 (s, 3H), 4.17-4.23 (m, 3H), 5.10-5.14 (m, 1H), 5.25-5.31 (m, 1H), 7.03 (d, J = 8.4 Hz, 1H), 7.33-7.42 (m, 2H), 7.84-7.89 (m, 1H), 8.22-8.32 (m, 3H), 8.55 (d, J = 8.0 Hz, 1H), 8.71 (s, 1H), 8.78 (d, J = 6.4 Hz, 1H), 9.78 (s, 1H), 10.05 (brs, 1H), 10.51 (brs, 1H), 11.11 (s, 1H).</a>                   |
| <a href="#">127</a> | <div>  </div> | <a href="#">C</a> | <a href="#">683.5</a> | <a href="#">1H NMR (400 MHz, DMSO-d6): δ 1.11-1.23 (m, 4H), 1.82-1.99 (m, 4H), 2.30-2.39 (m, 3H), 2.60 (br, 4H), 2.86-2.94 (m, 3H), 3.17 (s, 2H), 3.98 (s, 3H), 4.10 (br, 1H), 4.21 (d, J = 16.8 Hz, 1H), 4.32-4.41(m, 3H), 5.05 (dd, J = 13.2 Hz, 1H), 6.96 (d, J = 9.2 Hz, 1H), 7.06-7.08 (m, 2H), 7.53 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 6.0 Hz, 1H), 7.95 (s, 1H), 8.02 (dd, J = 9.2 Hz, 1H), 8.30 (dd, J = 8.4 Hz, 1H), 8.51 (d, J = 5.6 Hz, 1H), 8.64 (s, 1H), 9.38 (s, 1H), 10.95 (s, 1H).</a> |
| <a href="#">128</a> | <div>  </div> | <a href="#">C</a> | <a href="#">697.6</a> | <a href="#">1H NMR (400 MHz, DMSO-d6) δ 1.16-1.23 (m, 3H), 1.40-1.50 (m, 2H), 1.61 (br, 1H), 1.76-1.78 (m, 2H), 1.94-1.96 (m, 1H), 2.38-2.41 (s, 3H), 2.51-2.56 (m, 4H), 2.82-2.90 (m, 3H), 3.29-3.33 (m, 4H), 3.95 (s, 3H), 4.18-4.22 (m, 1H), 4.30-4.39 (m, 3H), 5.02-5.08 (m, 1H), 6.95</a>                                                                                                                                                                                                                                  |

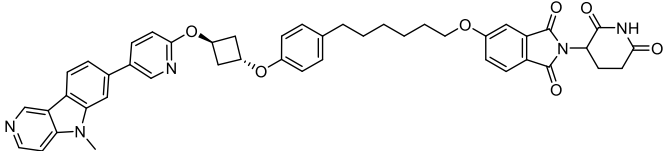
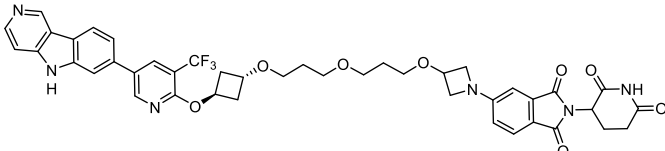
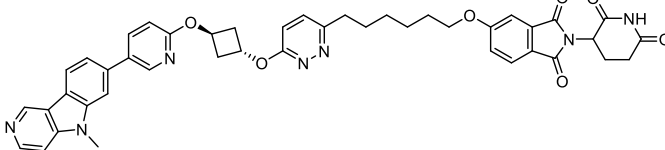


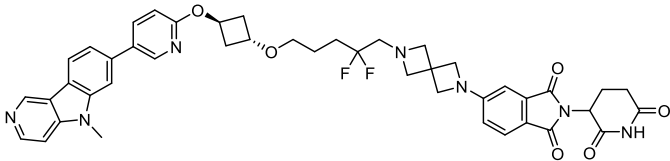
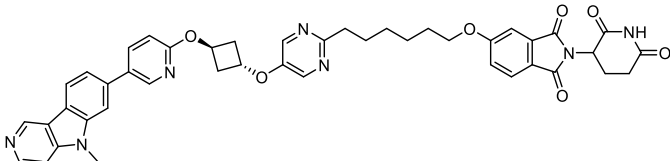
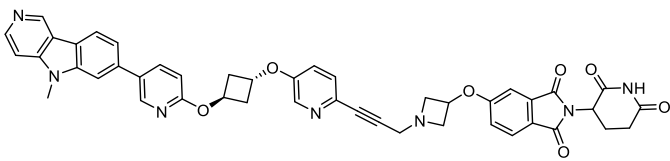
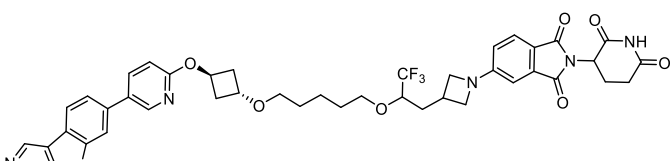


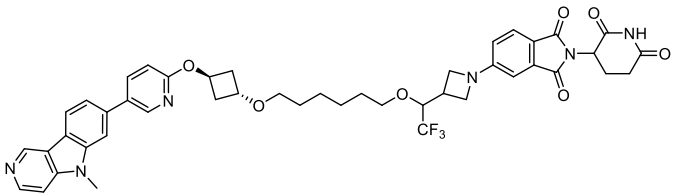
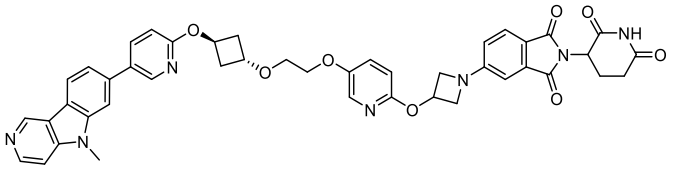
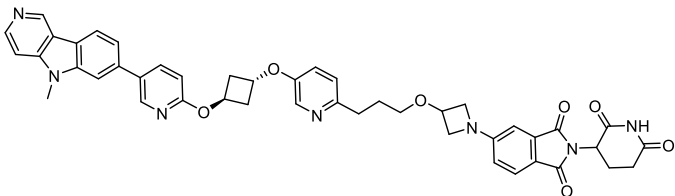


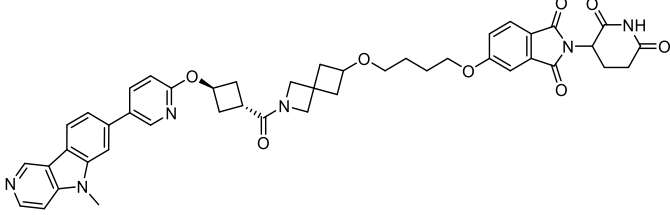
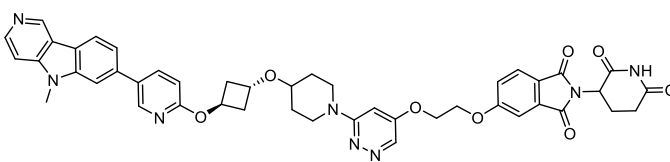
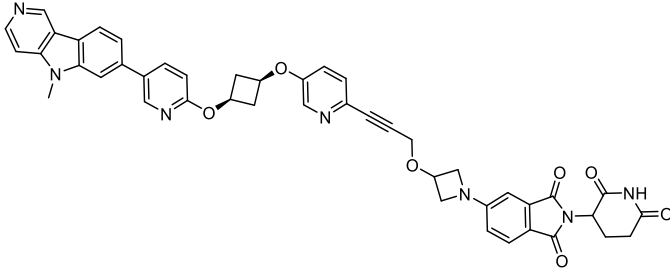
|            |                                                                                     |          |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|------------|-------------------------------------------------------------------------------------|----------|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|            |                                                                                     |          |              | Hz, 1H), 9.53 (s, 1H), 11.11 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <u>140</u> |    | <u>A</u> | <u>766.5</u> | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.99-2.05 (m, 1H), 2.26 (s, 3H), 2.52-2.60 (m, 2H), 2.89 (s, 1H), 3.48-3.65 (m, 12H), 3.74-3.83 (m, 4H), 4.04 (s, 3H), 4.24-4.31 (m, 2H), 4.44-4.50 (m, 2H), 5.08-5.13 (m, 1H), 7.32-7.34 (m, 1H), 7.41 (d, <i>J</i> = 2.0 Hz, 1H), 7.72 (d, <i>J</i> = 8.4 Hz, 1H), 7.79 (d, <i>J</i> = 8.4 Hz, 1H), 7.87 (d, <i>J</i> = 6.0 Hz, 1H), 8.04-8.10 (m, 2H), 8.40 (d, <i>J</i> = 8.0 Hz, 1H), 8.49 (d, <i>J</i> = 2.4 Hz, 1H), 8.61 (d, <i>J</i> = 6.4 Hz, 1H), 9.52 (s, 1H), 11.11 (s, 1H).                                                     |
| <u>141</u> |  | <u>C</u> | <u>776.5</u> | <sup>1</sup> H NMR (400 Hz, DMSO-d <sub>6</sub> ): δ 1.72-1.78 (m, 2H), 1.91-2.10 (m, 4H), 2.54-2.57 (m, 2H), 2.67-2.72 (m, 3H), 3.30 (s, 3H), 3.97 (s, 3H), 4.25 (t, <i>J</i> = 6.4 Hz, 2H), 5.11-5.18 (m, 2H), 5.41-5.48 (m, 1H), 7.01 (d, <i>J</i> = 8.8 Hz, 1H), 7.36 (dd, <i>J</i> = 8.8, 2.0 Hz, 1H), 7.46 (d, <i>J</i> = 2.0 Hz, 1H), 7.63-7.67 (m, 2H), 7.82 (d, <i>J</i> = 8.0 Hz, 1H), 8.01 (s, 1H), 8.23 (dd, <i>J</i> = 8.8, 2.4 Hz, 1H), 8.35 (d, <i>J</i> = 8.0 Hz, 1H), 8.44 (s, 2H), 8.52 (d, <i>J</i> = 5.6 Hz, 1H), 8.65 (d, <i>J</i> = 2.4 Hz, 1H), 9.39 (s, 1H), 11.12 (s, 1H). |
| <u>142</u> |  | <u>C</u> | <u>856.5</u> | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 1.90-1.94 (m, 2H), 1.99-2.04 (m, 1H), 2.34-2.40 (m, 1H), 2.65-2.70 (m, 4H), 3.46-3.50 (m, 1H), 3.55-3.61 (m, 2H), 3.86-3.90 (m, 1H), 3.96 (s, 3H), 4.89 (m, 2H), 4.95-5.01 (m, 2H), 5.24 (t, <i>J</i> = 4.6 Hz, 1H), 5.53-5.59 (m, 1H), 7.12-7.24 (m, 3H), 7.42 (d, <i>J</i> = 5.2 Hz, 1H), 7.60 (d, <i>J</i> = 8.0 Hz, 1H), 7.70-7.72 (m, 2H), 7.88 (s, 1H), 8.06 (d, <i>J</i> = 2.8 Hz, 1H), 8.28-8.30 (m, 2H), 8.42 (d, <i>J</i> = 6.4 Hz, 1H), 8.67 (d, <i>J</i> = 2.0 Hz, 1H), 9.29 (s, 1H).                                               |
| <u>143</u> |  | <u>B</u> | <u>820.5</u> | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 2.01-2.06 (m, 1H), 2.54-2.68 (m, 2H), 2.84-2.93 (m, 1H), 3.40-3.44 (m, 6H), 3.47-3.51 (m, 4H), 3.56-3.58 (m, 2H), 3.70 (br, 2H), 3.78-3.81 (m, 2H), 3.94 (s, 3H), 4.21 (br, 2H), 4.52 (t, <i>J</i> = 4.0 Hz, 2H), 5.11 (d, <i>J</i> = 12.8 Hz,                                                                                                                                                                                                                                                                                                |

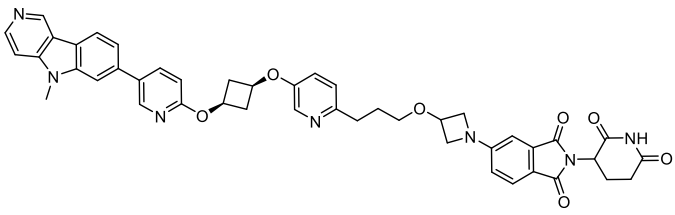
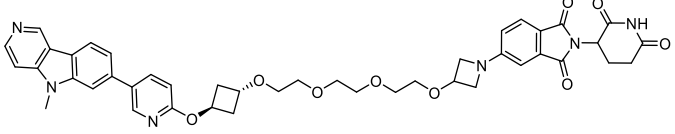
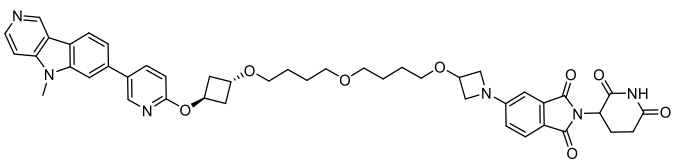
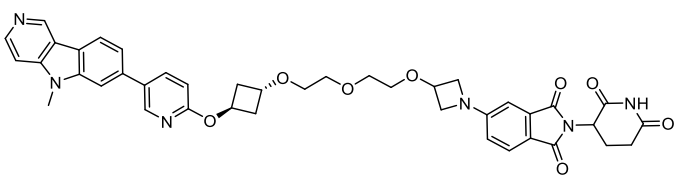
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|-----|-------------------------------------------------------------------------------------|---|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | <p>1H), 7.26 (d, <i>J</i> = 8.4 Hz, 1H), 7.34 (s, 1H), 7.64 (t, <i>J</i> = 6.8 Hz, 2H), 7.69 (d, <i>J</i> = 6.0 Hz, 1H), 7.74 (d, <i>J</i> = 8.4 Hz, 1H), 8.01 (s, 1H), 8.17 (d, <i>J</i> = 7.6 Hz, 1H), 8.34 (d, <i>J</i> = 8.4 Hz, 1H), 8.53 (d, <i>J</i> = 5.6 Hz, 1H), 9.40 (s, 1H), 11.12 (s, 1H).</p>                                                                                                                                                                                                                                                                                                                                                        |
| 144 |    | C | 775.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.68-1.75 (m, 2H), 1.88-1.95 (m, 2H), 2.03-2.08 (m, 1H), 2.16-2.23 (m, 2H), 2.52-2.65 (m, 3H), 2.85-2.93 (m, 1H), 3.08-3.14 (m, 2H), 3.31 (m, 1H), 3.96 (s, 3H), 4.24 (t, <i>J</i> = 6.4 Hz, 2H), 4.94-5.05 (m, 2H), 5.12 (dd, <i>J</i> = 5.2, 12.8 Hz, 1H), 6.81 (d, <i>J</i> = 8.8 Hz, 1H), 6.97 (d, <i>J</i> = 8.8 Hz, 1H), 7.36 (dd, <i>J</i> = 2.0, 8.4 Hz, 1H), 7.44 (d, <i>J</i> = 2.0 Hz, 1H), 7.61-7.70 (m, 3H), 7.82 (d, <i>J</i> = 8.0 Hz, 1H), 7.99 (s, 1H), 8.19-8.21 (m, 2H), 8.32 (d, <i>J</i> = 8.0 Hz, 1H), 8.51 (m, 1H), 8.65 (d, <i>J</i> = 2.0 Hz, 1H), 9.38 (m, 1H), 11.12 (s, 1H).</p> |
| 145 |  | C | 779.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.32-1.38 (m, 2H), 1.42-1.47 (m, 2H), 1.53-1.61 (m, 2H), 1.71-1.78 (m, 2H), 2.01-2.07 (m, 1H), 2.15-2.22 (m, 2H), 2.53-2.61 (m, 4H), 2.84-2.94 (m, 1H), 3.08-3.15 (m, 2H), 4.14-4.17 (m, 5H), 4.91-5.06 (m, 2H), 5.12 (dd, <i>J</i> = 5.6, 12.8 Hz, 1H), 6.78 (d, <i>J</i> = 8.4 Hz, 1H), 7.01 (d, <i>J</i> = 8.4 Hz, 1H), 7.33 (dd, <i>J</i> = 2.0, 8.4 Hz, 1H), 7.41 (d, <i>J</i> = 2.0 Hz, 1H), 7.61 (dd, <i>J</i> = 2.0, 8.4 Hz, 1H), 7.81-7.88 (m, 2H), 8.00 (d, <i>J</i> = 2.0 Hz, 1H), 8.20-8.28 (m, 3H), 8.56 (d, <i>J</i> = 8.4 Hz, 1H), 8.71-8.76 (m, 2H), 9.80 (s, 1H), 11.12 (s, 1H).</p>        |
| 146 |  | C | 763.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.67-1.75 (m, 2H), 1.87-1.97 (m, 2H), 2.03-2.07 (m, 1H), 2.20-2.23 (m, 2H), 2.53-2.67 (m, 4H), 2.85-2.94 (m, 1H), 3.98 (s, 3H), 4.23 (t, <i>J</i> = 6.0 Hz, 2H), 4.42-4.49 (m, 4H), 5.10-5.14 (m, 1H), 6.80 (d, <i>J</i> = 8.4 Hz, 1H), 6.96 (d, <i>J</i> = 5.2 Hz, 1H), 7.34-7.36 (m, 1H), 7.40 (d, <i>J</i> = 2.0 Hz, 1H), 7.63-7.69 (m, 3H), 7.82 (d, <i>J</i> = 8.4 Hz, 1H), 8.00 (s, 1H), 8.19-8.21 (m,</p>                                                                                                                                                                                             |

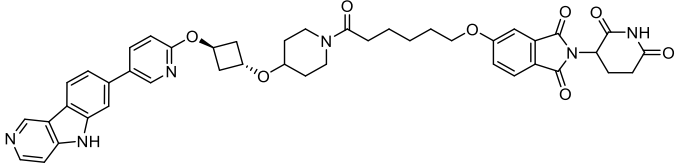
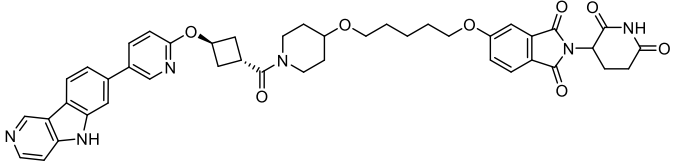
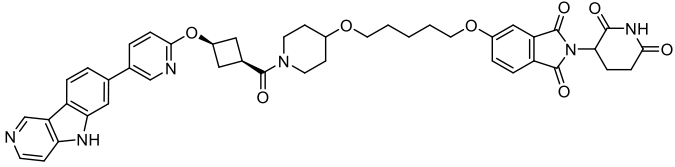
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|-----|-------------------------------------------------------------------------------------|---|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | <p>2H), 8.34 (d, <math>J</math> = 8.0 Hz, 1H), 8.51 (d, <math>J</math> = 6.0 Hz, 1H), 8.64 (d, <math>J</math> = 2.4 Hz, 1H), 9.40 (s, 1H), 11.12 (s, 1H).</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| 147 |    | C | 778.5 | <p><sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>): δ: 9.32(s, 1H), 8.58(d, <math>J</math> = 5.6 Hz, 1H), 8.49(s, 1H), 8.21(d, <math>J</math> = 8.0 Hz, 1H), 8.01(s, 1H), 7.92(d, <math>J</math> = 7.6 Hz, 1H), 7.77(d, <math>J</math> = 8.0 Hz, 1H), 7.56(s, 1H), 7.50(d, <math>J</math> = 8.0 Hz, 1H), 7.32(s, 2H), 7.17(d, <math>J</math> = 8.8 Hz, 1H), 7.08(d, <math>J</math> = 8.4 Hz, 2H), 6.86(d, <math>J</math> = 8.4 Hz, 1H), 6.75(d, <math>J</math> = 7.6 Hz, 2H), 5.49(s, 1H), 4.94(s, 2H), 4.07(t, <math>J</math> = 6.4 Hz, 2H), 3.91(s, 3H), 2.68-2.88(m, 8H), 2.57(t, <math>J</math> = 6.8 Hz, 2H), 2.01(s, 2H), 1.83(t, <math>J</math> = 6.8 Hz, 3H), 1.62-1.65(m, 2H).</p> |
| 148 |  | B | 827.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-<i>d</i><sub>6</sub>): δ 1.73-1.79 (m, 4H), 1.95-2.01 (m, 2H), 1.99-2.04 (m, 2H), 2.33-2.39 (m, 2H), 2.44-2.46 (m, 2H), 2.54-2.67 (m, 1H), 2.82-2.91 (m, 1H), 3.37-3.49 (m, 8H), 3.81-3.84 (m, 2H), 4.17-4.25(m, 3H), 4.43-4.48 (m, 1H), 5.01-5.06 (m, 1H), 5.45-5.50 (m, 1H), 6.61-6.64 (m, 1H), 6.77 (d, <math>J</math> = 4.8 Hz, 1H), 7.60 (d, <math>J</math> = 8.4 Hz, 1H), 7.73 (d, <math>J</math> = 6.8 Hz, 1H), 7.97 (s, 1H), 8.471-8.43 (m, 2H), 8.54 (d, <math>J</math> = 6.4 Hz, 1H), 8.85 (d, <math>J</math> = 4.8 Hz, 1H), 9.55 (s, 1H), 11.06 (s, 1H), 12.44 (s, 1H).</p>                                                               |
| 149 |  | B | 780.5 | <p><sup>1</sup>HNMR (400 MHz, DMSO-<i>d</i><sub>6</sub>): δ1.36-1.49 (m, 4H), 1.66-1.77 (m, 4H), 2.02-2.06 (m, 1H), 2.54-2.68 (m, 6H), 2.81-2.94 (m, 3H), 3.16-3.17 (m, 1H), 3.99 (s, 3H), 4.15-4.18 (m, 2H), 5.09-5.14(m, 1H), 5.44-5.53(m, 1H), 7.02 (d, <math>J</math> = 8.8 Hz, 1H), 7.16-7.18 (m, 1H), 7.33-7.35 (m, 1H), 7.45 (m, 1H), 7.54-7.56 (m, 1H), 7.65-7.67 (m, 1H), 7.72-7.73 (m, 1H), 7.81-7.83 (d, <math>J</math> = 8.0 Hz, 1H), 8.03 (s, 1H), 8.22-8.24(m, 1H), 8.35-8.37 (d, <math>J</math> = 8.0 Hz, 1H), 8.52-8.57(m, 1H), 8.64-8.65 (m, 1H), 9.42(s, 1H), 11.11 (s, 1H).</p>                                                                                       |

|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|-----|-------------------------------------------------------------------------------------|---|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 150 |    | B | 804.5 | <sup>1</sup> H NMR: (400 MHz, DMSO-d <sub>6</sub> ) δ: 10.95 (s, 1H), 9.14 (br s, 1H), 8.15 (s, 1H), 7.52 (d, J= 9.0 Hz, 1H), 7.18 - 7.04 (m, 5H), 6.83 (d, J= 6.7 Hz, 2H), 6.65 (d, J= 8.5 Hz, 1H), 6.61 (s, 1H), 6.54 - 6.47 (m, 3H), 6.26 (d, J= 8.5 Hz, 2H), 5.05 (dd, J= 5.0, 13.3 Hz, 1H), 4.38 - 4.26 (m, 1H), 4.24 - 4.11 (m, 1H), 3.78 (br t, J=6.5 Hz, 4H), 3.54 - 3.31 (m, 3H), 3.03 - 2.83 (m, 8H), 2.62 - 2.52 (m, 3H), 2.47 - 2.31 (m, 1H), 2.21 - 2.04 (m, 3H), 2.01 - 1.87 (m, 3H), 1.71 (br d, J=10.7 Hz, 2H). |
| 151 |  | B | 780.5 | <sup>1</sup> H NMR (400 Hz, DMSO-d <sub>6</sub> ): δ 11.21-1.26 (m, 1H), 1.33-1.48 (m, 4H), 1.69-1.73 (m, 4H), 1.01-2.07 (m, 1H), 2.57-2.68 (m, 5H), 2.79-2.93 (m, 3H), 4.02 (s, 3H), 4.16 (t, J= 6.4 Hz, 2H), 5.09-5.13 (m, 2H), 5.41-5.48 (m, 1H), 7.01 (d, J= 8.8 Hz, 1H), 7.35 (dd, J= 8.4, 1.6 Hz, 1H), 7.46 (d, J= 0.8 Hz, 1H), 7.69 (d, J= 8.0 Hz, 1H), 7.79-7.83 (m, 2H), 8.07 (s, 1H), 8.23 (dd, J= 8.4, 1.2 Hz, 1H), 8.37-8.45 (m, 3H), 8.58 (d, J= 6.0 Hz, 1H), 8.67 (s, 1H), 9.49 (s, 1H), 11.11 (s, 1H)..          |
| 152 |  | A | 788.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 2.01-2.06 (m, 1H), 2.53-2.73 (m, 6H), 2.84-2.92 (m, 1H), 3.59 (s, 2H), 3.81 (t, J= 6.8 Hz, 2H), 3.96 (s, 3H), 5.07-5.14 (m, 3H), 5.42-5.47 (m, 1H), 6.99 (d, J= 8.4 Hz, 1H), 7.28-7.33 (m, 3H), 7.48 (d, J= 8.4Hz, 1H), 7.62-7.65 (m, 2H), 7.84 (d, J= 8.0 Hz, 1H), 7.99 (s, 1H), 8.20-8.24 (m, 2H), 8.33 (d, J= 8.0 Hz, 1H), 8.51 (m, 1H), 8.65 (d, J= 2.4 Hz, 1H), 9.38 (m, 1H), 11.11 (s, 1H).                                                                         |
| 153 |  | B | 839.6 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.38-1.41 (m, 2H), 1.54-1.59 (m, 4H), 1.92-1.96 (m, 3H), 2.23-2.45 (m, 5H), 2.82-3.02 (m, 2H), 3.34 (t, J= 6.0 Hz, 2H), 3.56-3.62 (m, 1H), 3.67-3.79 (m, 3H), 4.04-4.05 (m, 1H), 4.14-4.21 (m, 6H), 5.01-5.06 (m, 1H), 5.29-5.35 (m, 1H), 6.61 (d, J= 8.0 Hz, 1H), 6.74 (s, 1H), 6.96 (d, J= 8.4 Hz,                                                                                                                                                                      |

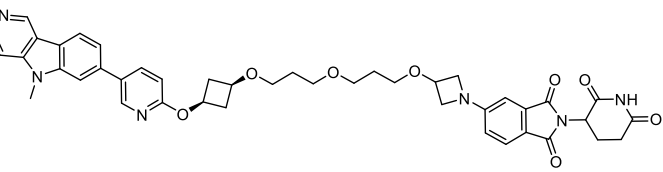
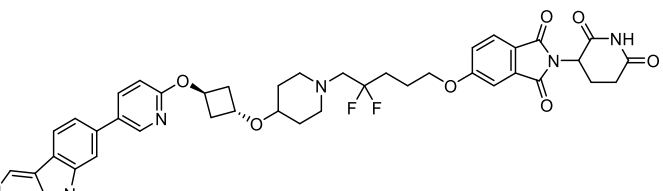
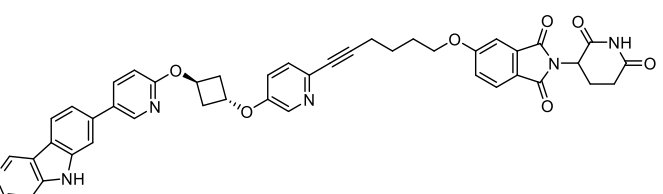
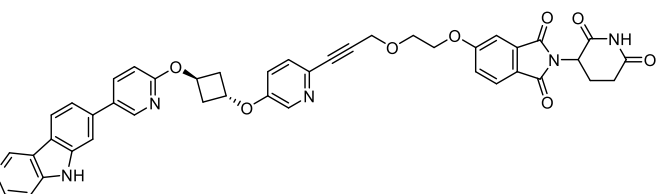
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-----|-------------------------------------------------------------------------------------|---|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | 1H), 7.61 (d, J = 8.0 Hz, 1H),<br>7.86 (d, J = 8.0 Hz, 1H),<br>8.21-8.25 (m, 3H), 8.53 (d, J<br>= 8.4 Hz, 1H), 8.68 (d, J = 1.6<br>Hz, 1H), 8.77 (d, J = 6.8 Hz,<br>1H), 9.77 (s, 1H), 11.07 (s,<br>1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| 154 |    | C | 839.6 | 1HNMR (400 MHz, DMSO-<br>d6): δ 1.26 (s, 4H), 1.36-1.37<br>(m, 2H), 1.49-1.54 (m, 2H),<br>1.97-2.00 (m, 1H), 2.29-2.42<br>(m, 4H), 2.53-2.59 (m, 2H),<br>2.83-2.91 (m, 1H), 3.17-3.23<br>(m, 3H), 3.65-3.71 (m, 1H),<br>3.78-3.89 (m, 2H), 3.96 (s,<br>3H), 3.98-4.02 (m, 1H),<br>4.11-4.22 (m, 3H), 4.33-4.36<br>(m, 1H), 5.04-5.08 (m, 1H),<br>5.28-5.34 (m, 1H), 6.68-6.70<br>(m, 1H), 6.83-6.84 (m, 1H),<br>6.93-6.95 (m, 1H), 7.61-7.66<br>(m, 3H), 7.98 (s, 1H), 8.17-<br>8.20 (m, 1H), 8.31-8.33 (m,<br>1H), 8.49-8.51 (m, 1H),<br>8.63-8.64 (m, 1H), 9.36 (s,<br>1H), 11.07 (s, 1H).                                                            |
| 155 |  | C | 794.5 | 1H NMR (400 MHz,<br>DMSO-d6): δ 2.33-2.50<br>(m,6H), 2.54-2.60 (m, 1H),<br>2.83-2.93 (m, 1H), 3.68 (t, J<br>= 4.4 Hz, 2H), 3.96 (s, 3H),<br>4.01 (d, J = 3.6 Hz, 2H), 4.15<br>(t, J = 4.0 Hz, 2H), 4.28-<br>4.33(m, 1H), 4.45-4.49<br>(m,2H), 4.04 (s, 1H), 5.06 (d,<br>J = 5.2 Hz,1H), 5.31-5.36 (m<br>,1H), 5.43-5.48 (m,1H),<br>6.71(dd, J = 2.0 Hz,1H),6.88<br>(t, J = 9.2 Hz,2H), 6.95 (d, J<br>= 8.8 Hz,1H), 7.50 (d, J = 3.2<br>Hz, 1H), 7.61-7.65 (m, 1H),<br>7.91 (d, J = 2.8 Hz,1H), 7.99<br>(s,1H), 8.18-8.20 (m ,1H),<br>8.33 (d, J = 8.0 Hz ,1H), 8.50<br>(d, J = 6.0 Hz, 1H), 8.65 (d, J<br>= 2.4 Hz,1H), 9.37 (s, 1H),<br>11.08 (s, 1H). |
| 156 |  | C | 792.5 | 1H NMR (400 MHz,<br>DMSO-d6): δ 1.93-2.01 (m,<br>3H), 2.54-2.70 (m, 6H), 2.85<br>(t, J = 7.2 Hz, 2H), 3.45 (t, J<br>= 6 Hz, 2H), 3.79-3.81 (m,<br>2H), 4.15 (s, 3H), 4.22-4.26<br>(m, 2H), 4.43-4.45 (m, 1H),<br>5.03-5.10 (m, 3H), 5.43-5.46<br>(m, 1H), 6.67 (d, J = 8.4 Hz,<br>1H), 6.81 (s, 1H), 7.04 (d, J =<br>8.4 Hz, 1H), 7.46-7.56 (m,<br>2H), 7.65(d, J = 8.4 Hz, 1H),<br>7.88 (d, J = 8.4 Hz, 1H),<br>8.21-8.30 (m, 4H), 8.55 (d, J<br>= 8 Hz,1H), 8.71-8.79 (m,                                                                                                                                                                             |

|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-----|-------------------------------------------------------------------------------------|---|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | 2H), 9.77 (s, 1H), 11.07 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 157 |    | C | 797.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.61-1.66 (m, 2H), 1.75-1.82 (m, 2H), 1.99-2.06 (m, 4H), 2.29-2.33 (m, 2H), 2.43-2.45 (m, 3H), 2.55-2.61 (m, 3H), 2.56-2.93 (m, 1H), 3.06-3.09 (m, 1H), 3.31 (s, 1H), 3.80-3.88 (m, 3H), 3.96 (s, 3H), 4.00-4.06 (m, 2H), 4.18 (t, J = 7.4 Hz, 2H), 5.10-5.14 (m, 1H), 5.28-5.33 (m, 1H), 6.93 (d, J = 8.8 Hz, 1H), 7.33-7.36 (m, 1H), 7.42 (d, J = 1.6 Hz, 1H), 7.61-7.64 (m, 2H), 7.83 (d, J = 8.4 Hz, 1H), 7.98 (s, 1H), 8.18-8.20 (m, 1H), 8.32 (d, J = 8.0 Hz, 1H), 8.50 (d, J = 5.6 Hz, 1H), 8.63 (d, J = 2.0 Hz, 1H), 9.37 (s, 1H), 11.12 (s, 1H) |
| 158 |  | C | 823.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.45-1.47 (m, 2H), 1.89-1.92 (m, 2H), 1.97-2.07 (m, 3H), 2.40-2.44 (m, 4H), 2.55-2.67 (m, 1H), 2.84-2.94 (m, 1H), 3.16-3.25 (m, 2H), 3.56-3.64 (m, 1H), 4.05 (s, 3H), 4.10-4.13 (m, 2H), 4.42-4.45 (m, 1H), 4.51-4.58 (m, 3H), 5.10-5.15 (m, 1H), 5.31-5.35 (m, 1H), 6.78 (s, 1H), 6.97 (d, J = 8.8 Hz, 1H), 7.40-7.42 (m, 1H), 7.51 (s, 1H), 7.85-7.89 (m, 2H), 8.10 (s, 1H), 8.21-8.24 (m, 1H), 8.35 (d, J = 1.6 Hz, 1H), 8.42 (d, J = 8.4 Hz, 1H), 8.62 (d, J = 6.0 Hz, 1H), 8.67 (d, J = 2.4 Hz, 1H), 9.54 (s, 1H), 11.12 (s, 1H).                   |
| 159 |  | C | 788.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.99-2.03 (m, 2H), 2.21-2.24 (m, 2H), 2.54-2.67 (m, 2H), 2.83-2.92 (m, 1H), 3.16-3.27 (m, 2H), 3.95-3.98 (m, 4H), 3.30-3.34 (m, 2H), 4.49 (s, 2H), 4.66-4.72 (m, 2H), 5.01-5.08 (m, 2H), 6.68 (d, J = 8.4 Hz, 1H), 6.82 (s, 1H), 6.98 (d, J = 8.4 Hz, 1H), 7.37 (dd, J = 8.4 Hz, 1H), 7.54 (d, J = 8.8 Hz, 1H), 7.62-7.67 (m, 3H), 7.99 (s, 1H), 8.21 (d, J = 8.4 Hz, 1H), 8.26 (d, J = 2.8 Hz, 1H), 8.33 (d, J = 8.4 Hz, 1H), 8.50 (d, J = 5.6 Hz, 1H), 8.65 (d, J = 2.0 Hz, 1H), 9.37 (s, 1H), 11.07 (s, 1H).                                          |

|     |                                                                                                  |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|-----|--------------------------------------------------------------------------------------------------|---|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 160 | <div>  </div>   | B | 792.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.88-1.95 (m, 2H), 1.97-2.03 (m, 2H), 2.16-2.23 (m, 2H), 2.54-2.60 (m, 1H), 2.67-2.76 (m, 2H), 2.83-2.92 (m, 1H), 3.14-3.21 (m, 2H), 3.43 (t, J = 6.4 Hz, 2H), 3.84 (d, J = 8.8 Hz, 2H), 3.97 (s, 3H), 4.23-4.27 (m, 2H), 4.43-4.48 (m, 1H), 4.56-4.63 (m, 1H), 5.00-5.08 (m, 2H), 6.66 (d, J = 8.0 Hz, 1H), 6.81 (s, 1H), 6.98 (d, J = 8.8 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 7.24-7.27 (m, 1H), 7.62-7.66 (m, 3H), 8.00 (s, 1H), 8.16 (d, J = 2.8 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 8.33 (d, J = 8.0 Hz, 1H), 8.51 (d, J = 5.6 Hz, 1H), 8.65 (d, J = 2.4 Hz, 1H), 9.38 (s, 1H), 11.07 (s, 1H).</p> |
| 161 | <div>  </div> | C | 789.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 2.30-2.36 (m, 2H), 2.40-2.46 (m, 3H), 2.54-2.58 (m, 2H), 2.82-2.91 (m, 1H), 3.44-3.47 (m, 2H), 3.54-3.57 (m, 10H), 3.85 (d, J = 9.2Hz, 2H), 3.95 (s, 3H), 4.20-4.25 (m, 3H), 4.48-4.50 (m, 1H), 5.04 (t, J = 12.8 Hz, 1H), 5.28-5.33 (m, 1H), 6.62 (d, J = 8.4 Hz, 1H), 6.77 (d, J = 2.0 Hz, 1H), 6.93 (d, J = 8.8 Hz, 1H), 7.60-7.62 (m, 3H), 7.97 (s, 1H), 8.17-8.20 (m, 1H), 8.49 (d, J = 6.0 Hz, 1H), 8.63 (d, J = 2.4 Hz, 1H), 9.36 (s, 1H), 11.07 (s, 1H).</p>                                                                                                                                  |
| 162 | <div>  </div> | A | 801.6 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.56 (s, 8H), 1.98-2.01 (m, 1H), 2.34-2.46 (m, 6H), 2.59-2.67 (m, 2H), 2.83-2.92 (m, 1H), 3.38-3.42 (m, 6H), 3.83 (d, J = 5.6 Hz, 2H), 3.96 (s, 3H), 4.18-4.25 (m, 3H), 4.44 (s, 1H), 5.03-5.07 (m, 1H), 5.29-5.33 (m, 1H), 6.63 (d, J = 7.6 Hz, 1H), 6.78 (s, 1H), 6.93 (d, J = 8.8 Hz, 1H), 7.61-7.63 (m, 3H), 7.98 (s, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.31 (d, J = 8.0 Hz, 1H), 8.49 (d, J = 5.6 Hz, 1H), 8.64 (s, 1H), 9.36 (s, 1H), 11.07 (s, 1H).</p>                                                                                                                                           |
| 163 | <div>  </div> | C | 745.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.94-2.00 (m, 1H), 2.31-2.48 (m, 4H), 3.97 (s, 3H), 2.57 (s, 2H), 2.81-2.89 (m, 1H), 3.47-3.49 (m, 2H), 3.54-3.64 (m, 6H).</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |

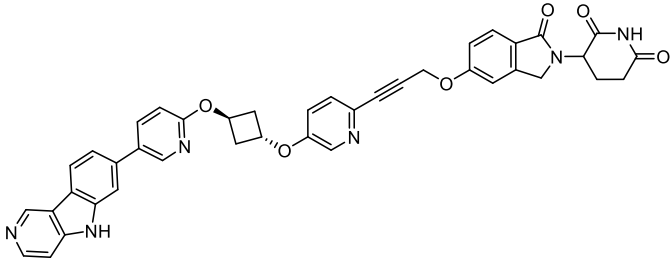
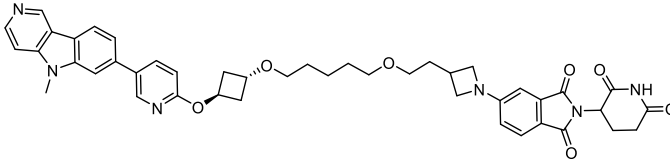
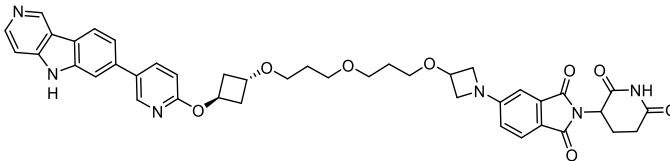
|                     |                                                                                                  |                   |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|---------------------|--------------------------------------------------------------------------------------------------|-------------------|-----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                     |                                                                                                  |                   |                       | <a href="#">3.84-3.89 (m, 2H), 4.21-4.29 (m, 3H), 4.52 (s, 1H), 5.02-5.06 (m, 1H), 5.29-5.35 (s, 1H), 6.63-6.66 (m, 1H), 6.79 (d, J = 2.0 Hz, 1H), 6.93 (d, J = 8.8 Hz, 1H), 7.59-7.66 (m, 2H), 7.69 (d, J = 6.0 Hz, 1H), 7.99 (s, 1H), 8.17-8.20 (m, 1H), 8.34 (d, J = 8.0 Hz, 1H), 8.53 (d, J = 6.0 Hz, 1H), 8.62 (d, J = 2.4 Hz, 1H), 9.40 (s, 1H), 11.07 (s, 1H).</a>                                                                                                                                                                                                                                                                   |
| <a href="#">164</a> | <div>  </div>  | <a href="#">C</a> | <a href="#">785.5</a> | <a href="#">1H NMR (400 MHz, CDCl<sub>3</sub>): δ 1.52-1.57 (m, 3H), 1.61-1.65 (m, 2H), 1.70-1.74 (m, 2H), 1.98-2.01 (m, 2H), 2.13-2.17 (m, 1H), 2.34-2.41 (m, 2H), 2.47-2.50 (m, 2H), 2.78-2.88 (m, 2H), 3.20-3.28 (m, 2H), 3.54-3.72 (m, 3H), 4.00-4.10 (m, 3H), 4.39-4.44 (m, 1H), 4.95 (dd, J = 5.2, 12.0 Hz, 1H), 5.31-5.42 (m, 4H), 6.82 (d, J = 8.4 Hz, 1H), 7.17 (d, J = 8.8Hz, 1H), 7.31-7.34 (m, 2H), 7.48-7.51 (m, 2H), 7.68 (s, 1H), 7.77 (d, J = 8.8 Hz, 1H), 7.87 (d, J = 7.2 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 8.32 (s, 1H), 8.41-8.45 (m, 2H), 9.23 (s, 1H).</a>                                                           |
| <a href="#">165</a> | <div>  </div> | <a href="#">C</a> | <a href="#">785.5</a> | <a href="#">1HNMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.35-1.38 (m, 2H), 1.47-1.57 (m, 4H), 1.74-1.81 (m, 4H), 1.99-2.07 (m, 2H), 2.32-2.39 (m, 2H), 2.57 (s, 1H), 2.62-2.67 (m, 2H), 2.82-2.91 (m, 1H), 3.12-3.18 (m, 3H), 3.41-3.51 (m, 4H), 3.85-3.89 (m, 1H), 4.17-4.20 (m, 2H), 5.09-5.14 (m, 1H), 5.18-5.22 (m, 1H), 6.92 (d, J = 8.4 Hz, 1H), 7.33-7.36 (m, 1H), 7.42 (d, J = 1.6 Hz, 1H), 7.47 (d, J = 5.6 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.76 (s, 1H), 7.82 (d, J = 8.4 Hz, 1H), 8.10-8.12 (m, 1H), 8.29 (d, J = 8.0 Hz, 1H), 8.42 (d, J = 6.0 Hz, 1H), 8.54 (d, J = 2.4 Hz, 1H), 9.35 (s, 1H), 11.11 (s, 1H), 11.81 (s, 1H).</a> |
| <a href="#">166</a> | <div>  </div> | <a href="#">C</a> | <a href="#">785.5</a> | <a href="#">1H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.31-1.37 (m, 2H), 1.48-1.50 (m, 2H), 1.55-1.57 (m, 2H), 1.76-1.79 (m, 4H), 2.03-2.06 (m, 1H), 2.18-2.27 (m, 2H), 2.55-2.70 (m, 3H), 2.85-2.92 (m, 1H), 3.06-3.17 (m, 4H), 3.42-3.48 (m, 3H), 3.57-3.60 (m, 1H), 3.79-3.83 (m, 1H), 4.17 (t, J</a>                                                                                                                                                                                                                                                                                                                                      |

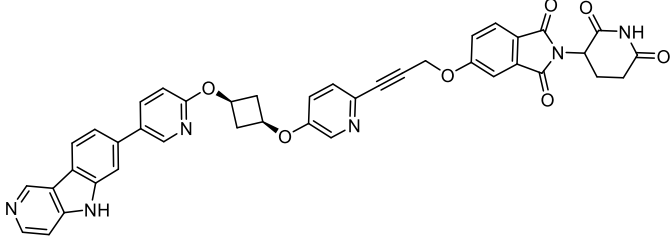
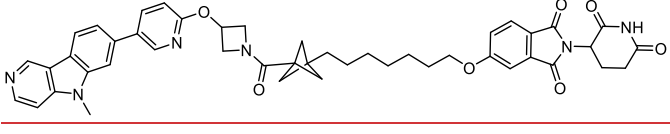
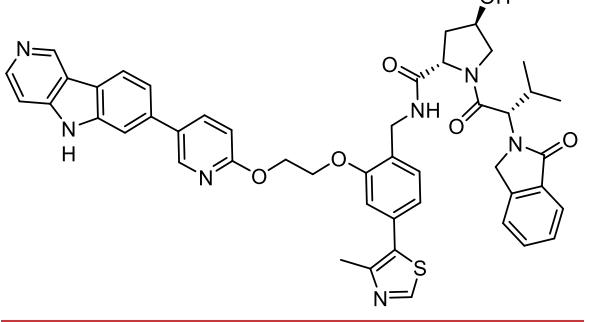


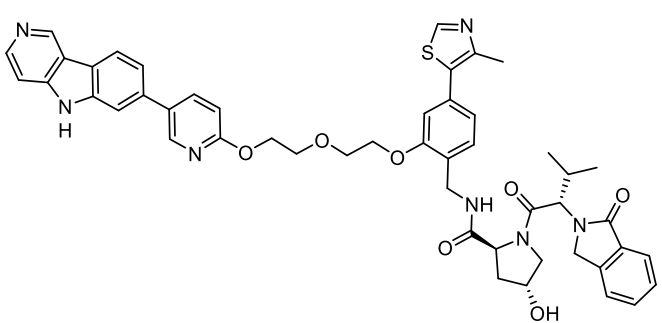
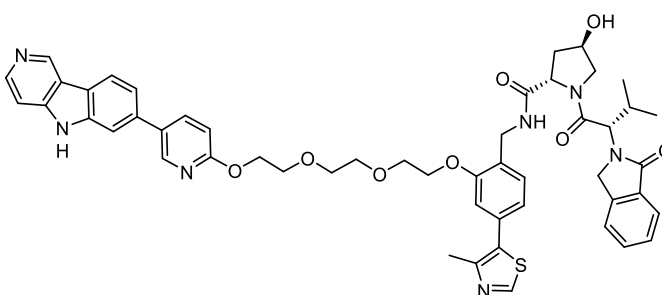
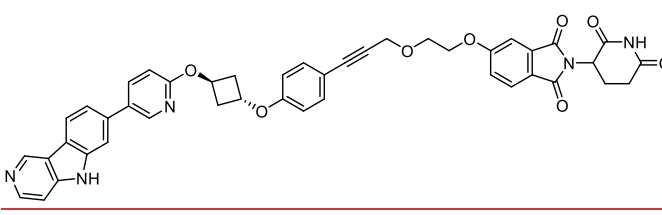
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|-----|-------------------------------------------------------------------------------------|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | (m, 1H), 11.07 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| 170 |    | A | 773.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.71-1.77 (m, 4H), 1.94-1.97 (m, 3H), 2.54-2.58 (m, 1H), 2.86-2.88 (m, 3H), 3.16 (d, J = 3.6 Hz, 1H), 3.38-3.46 (m, 8H), 3.75 (d, J = 6.8 Hz, 1H), 3.80-3.84 (m, 2H), 4.03 (s, 3H), 4.19-4.23 (m, 2H), 4.41-4.42 (m, 1H), 4.83-4.90 (m, 1H), 5.01-5.06(m, 1H), 6.61-6.63 (m, 1H), 6.76 (d, J = 0.8 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 6.0 Hz, 1H), 8.08 (s, 1H), 8.20-8.22 (m, 1H), 8.41 (d, J = 8.0 Hz, 1H), 8.61 (d, J = 6.4 Hz, 1H), 8.66 (d, J = 2.4 Hz, 1H), 9.55 (s, 1H), 11.06 (s, 1H). |
| 171 |  | C | 807.5 | <sup>1</sup> H NMR: (400MHz, DMSO-d <sub>6</sub> )<br>δ = 11.11 ( s, 1H), δ = 9.35 (s, 1H) δ = 8.64 (s, 1H), 8.49 – 8.48 (d, J = 4 Hz 1H), 8.33 – 8.31 (d, J = 8 Hz 1H), δ = 8.17 (s, 1H), δ = 7.97 (s, 1H), 7.85 – 7.83 (d, J = 8 Hz 1H), 7.62 – 7.61 (d, J = 4 Hz 2H), 7.43 (s, 1H), 6.94 – 6.92 (d, J = 8 Hz 1H), 5.31 - 5.29 (m, 1H), 5.12 – 5.10 (m, 1H), 4.34 (s, 5H), 4.25-4.23 (d, J = 8 Hz 1H), 3.95 ( s, 3H), 2.77 (m, 2H), 2.73 (m, 4H), 2.53-2.52 (m, 1H), 2.39-2.38 (m, 4H), 1.91 - 1.90 (m, 4H), 1.75 (m, 2H), 1.43 ( m, 2H), 1.41 (m, 2H).                                                             |
| 172 |  | C | 761.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.68-1.77 (m, 2H), 1.89-1.96 (m, 2H), 2.02-2.08 (m, 1H), 2.53-2.69 (m, 8H), 2.85-2.94 (m, 1H), 4.25 (t, J = 6.2 Hz, 2H), 5.41-5.47 (m, 1H), 7.01 (d, J = 8.4 Hz, 1H), 7.26-7.45 (m, 4H), 7.80-7.84 (m, 2H), 7.99-8.03 (m, 2H), 8.18-8.21 (m, 2H), 8.51-8.68 (m, 3H), 9.77 (s, 1H), 11.11 (s, 1H), 13.17 (s, 1H).                                                                                                                                                                                                                                                |
| 173 |  | A | 763.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 2.02-2.08 (m, 1H), 2.52-2.76 (m, 6H), 2.85-2.93 (m, 1H), 3.89-3.95 (m, 2H), 4.37-4.42 (m, 2H), 4.49 (s, 2H), 5.06-5.14 (m, 2H), 5.40-5.47 (m, 1H), 6.99 (d, J = 8.4 Hz, 1H), 7.30-7.33 (m,                                                                                                                                                                                                                                                                                                                                                                      |

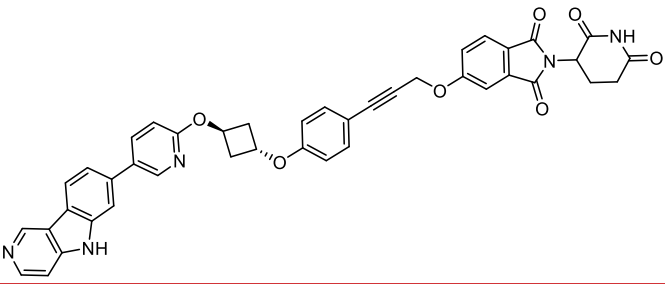
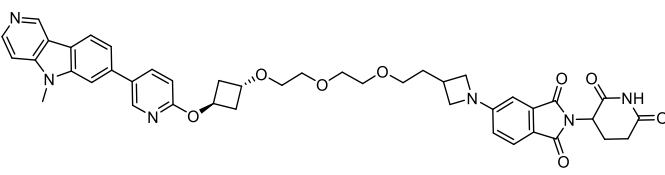
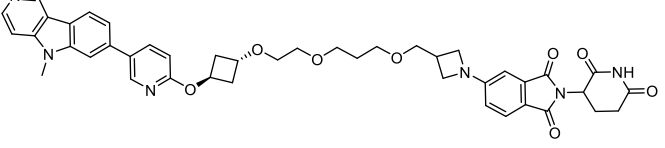
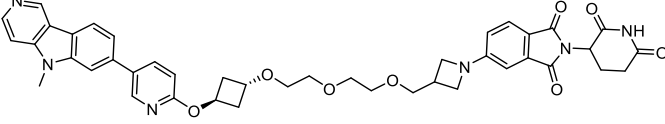


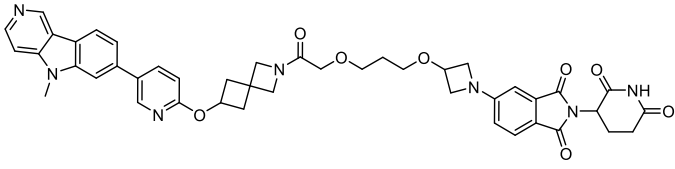
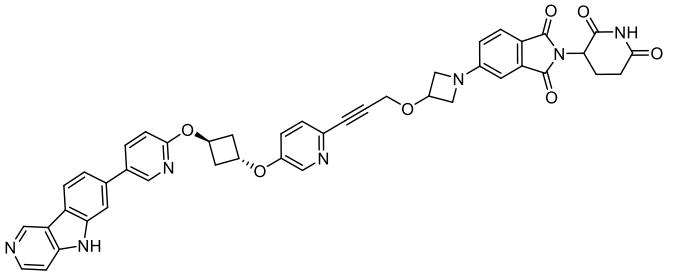
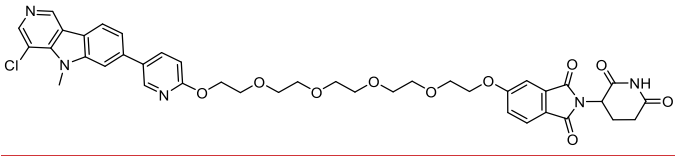


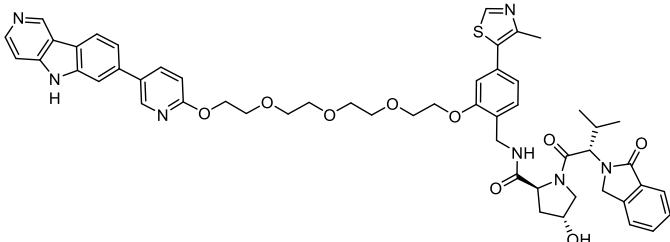
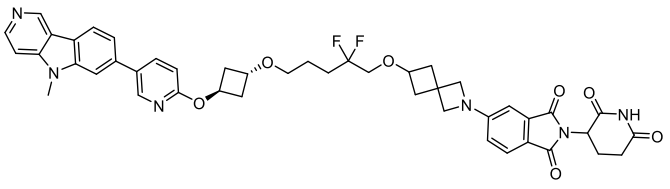
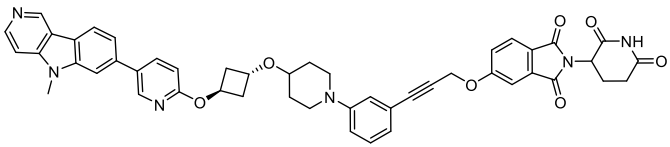
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-----|-------------------------------------------------------------------------------------|---|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 180 |    | A | 705.4 | <sup>1</sup> HNMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.97-2.00 (m, 1H), 2.33-2.44 (m, 2H), 2.55-2.67 (m, 4H), 2.86-2.96 (m, 1H), 4.29 (d, <i>J</i> = 17.2 Hz, 1H), 4.42 (d, <i>J</i> = 16.8 Hz, 1H), 5.06-5.10 (m, 2H), 5.18 (s, 2H), 5.42-5.45 (m, 1H), 6.99 (d, <i>J</i> = 8.4 Hz, 1H), 7.17 (d, <i>J</i> = 8.0 Hz, 1H), 7.29-7.33 (m, 2H), 7.50 (d, <i>J</i> = 8.4 Hz, 1H), 7.68 (d, <i>J</i> = 8.0 Hz, 2H), 7.74 (d, <i>J</i> = 5.6 Hz, 1H), 7.89 (s, 1H), 8.16 (d, <i>J</i> = 7.6 Hz, 1H), 8.24 (s, 1H), 8.41 (d, <i>J</i> = 7.6 Hz, 1H), 8.53-8.59 (m, 2H), 9.56 (s, 1H), 10.97 (s, 1H), 12.54 (br, 1H).                                 |
| 181 |  | B | 771.6 | <sup>1</sup> HNMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.34-1.41 (m, 2H), 1.48-1.57 (m, 4H), 1.84-1.89 (m, 2H), 1.95-1.99 (m, 1H), 2.31-2.46 (m, 5H), 2.54-2.58 (m, 2H), 2.79-2.92 (m, 2H), 3.35-3.42 (m, 4H), 3.68-3.71 (m, 2H), 3.95 (s, 3H), 4.11-4.19 (m, 3H), 5.01-5.05 (m, 1H), 5.29-5.35 (m, 1H), 6.59 (d, <i>J</i> = 8.0 Hz, 1H), 6.73 (s, 1H), 6.93 (d, <i>J</i> = 8.0 Hz, 1H), 7.59-7.62 (m, 3H), 7.96 (s, 1H), 8.16-8.19 (m, 1H), 8.30-8.32 (d, <i>J</i> = 8.0 Hz, 1H), 8.49 (d, <i>J</i> = 8.0 Hz, 1H), 8.61-8.62 (m, 1H), 9.35 (s, 1H), 11.06 (s, 1H).                                                                              |
| 182 |  | A | 759.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.73-1.79 (m, 4H), 1.97-2.00 (m, 1H), 2.33-2.45 (m, 5H), 2.54-2.58 (m, 1H), 2.82-2.90 (m, 1H), 3.37 (t, <i>J</i> = 6.4 Hz, 2H), 3.43-3.49 (m, 6H), 3.81-3.84 (m, 2H), 4.16-4.20 (m, 1H), 4.22-4.26 (m, 2H), 4.43-4.47 (m, 1H), 5.02-5.06 (m, 1H), 5.31-5.34 (m, 1H), 6.63 (d, <i>J</i> = 8.4 Hz, 1H), 6.78 (s, 1H), 6.93 (d, <i>J</i> = 8.4 Hz, 1H), 7.60-7.65 (m, 2H), 7.72 (d, <i>J</i> = 6.0 Hz, 1H), 7.86 (s, 1H), 8.11-8.14 (m, 1H), 8.39 (d, <i>J</i> = 8.4 Hz, 1H), 8.53 (d, <i>J</i> = 6.0 Hz, 1H), 8.57 (d, <i>J</i> = 2.0 Hz, 1H), 9.53 (s, 1H), 11.06 (s, 1H), 12.42 (s, 1H). |

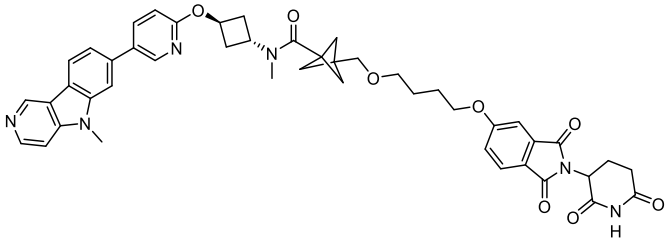
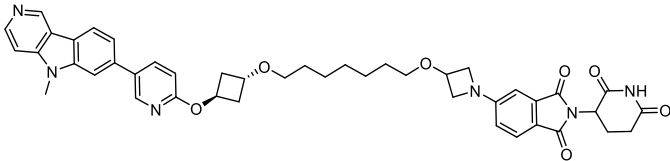
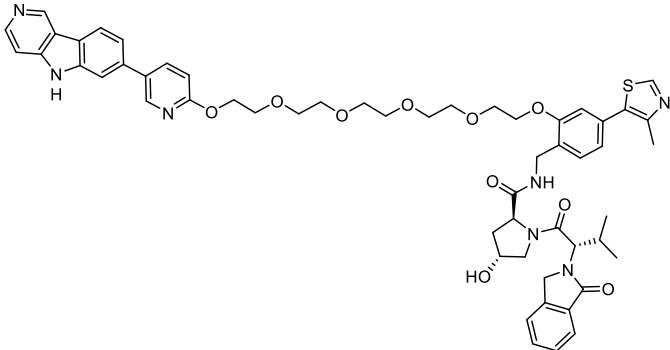
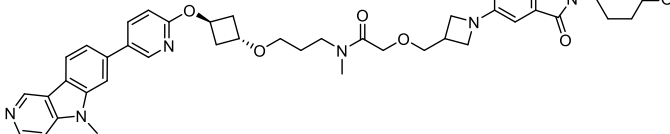
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-----|-------------------------------------------------------------------------------------|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 183 |    | A | 719.4 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 2.03-2.07 (m, 1H), 2.18-2.24 (m, 2H), 2.54-2.62 (m, 1H), 2.84-2.94 (m, 1H), 3.17-3.20 (m, 3H), 4.67 (t, <i>J</i> = 6.4 Hz, 1H), 5.01 (t, <i>J</i> = 6.8 Hz, 1H), 5.11-5.15 (m, 1H), 5.32 (s, 2H), 6.97(d, <i>J</i> = 8.4 Hz, 1H), 7.33-7.36 (m, 1H), 7.45-7.52 (m, 2H), 7.58 (d, <i>J</i> = 1.6 Hz, 1H), 7.68 (d, <i>J</i> = 8.0 Hz, 1H), 7.74 (d, <i>J</i> = 5.6 Hz, 1H), 7.89 (s, 1H), 7.91 (s, 1H), 8.14-8.16 (m, 1H), 8.25 (d, <i>J</i> = 2.8 Hz, 1H), 8.41 (d, <i>J</i> = 8.4 Hz, 1H), 8.54-8.55 (m, 1H), 8.58 (d, <i>J</i> = 2.4 Hz, 1H), 9.56 (s, 1H), 11.12 (s, 1H), 12.49 (s, 1H).                                 |
| 184 |  | A | 795.6 | <sup>1</sup> H NMR (400 Hz, DMSO-d <sub>6</sub> ): δ1.30-1.50 (m, 8H), 1.72-1.79 (m, 2H), 1.84 (s, 6H), 1.97-2.06 (m, 2H), 2.56-2.67 (m, 2H), 2.84-2.93 (m, 1H), 3.85-3.88 (m, 1H), 3.99 (s, 3H), 4.13-4.18 (m, 3H), 4.21-4.24 (m, 1H), 4.29-4.33 (m, 1H), 4.67-4.71 (m, 1H), 5.09-5.13 (m, 1H), 5.41-5.45 (m, 1H), 7.06 (d, <i>J</i> = 8.8 Hz, 1H), 7.34 (d, <i>J</i> = 8.0 Hz, 1H), 7.41 (s, 1H), 7.66 (d, <i>J</i> = 8.4 Hz, 1H), 7.62 (d, <i>J</i> = 5.6 Hz, 1H), 7.82 (d, <i>J</i> = 8.4 Hz, 1H), 8.04 (s, 1H), 8.23-8.29 (m, 1H), 8.37 (d, <i>J</i> = 8.0 Hz, 1H), 8.55 (d, <i>J</i> = 5.6 Hz, 1H), 8.66 (s, 1H), 9.44 (s, 1H), 11.11 (s, 1H)..                             |
| 185 |  | C | 836.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 0.67 (d, <i>J</i> = 6.8 Hz, 3H), 0.83-0.88 (m, 3H), 1.97-2.02 (m, 2H), 2.31-2.33 (m, 1H), 2.46 (s, 3H), 3.51 (s, 1H), 3.66-3.72 (m, 2H), 4.22-4.26 (m, 2H), 4.34-4.42 (m, 4H), 4.49-4.51 (m, 2H), 4.68 (d, <i>J</i> = 10.0 Hz, 1H), 5.05 (d, <i>J</i> = 4.4 Hz, 1H), 5.32 (t, <i>J</i> = 4.8 Hz, 1H), 6.58 (d, <i>J</i> = 9.6 Hz, 1H), 6.99 (d, <i>J</i> = 7.2 Hz, 1H), 7.06 (s, 1H), 7.31 (d, <i>J</i> = 8.0 Hz, 1H), 7.47-7.53 (m, 2H), 7.58-7.63 (m, 4H), 7.69 (d, <i>J</i> = 6.8 Hz, 1H), 7.77 (s, 1H), 7.96-7.99 (m, 1H), 8.31-8.33 (m, 2H), 8.40 (m, 1H), 8.48 (d, <i>J</i> = 6.0Hz, 1H), 8.98 (s, 1H), 9.45 (s, 1H). |

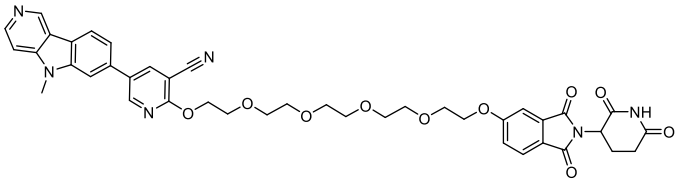
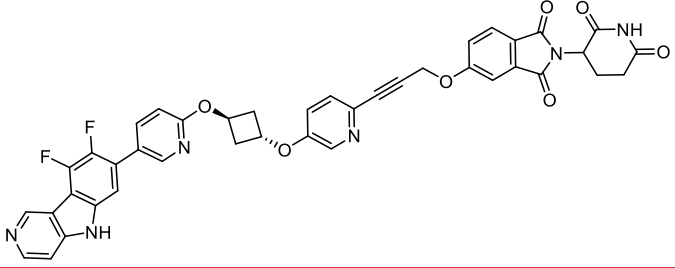
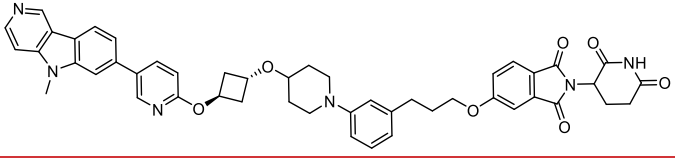
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-----|-------------------------------------------------------------------------------------|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 186 |    | B | 880.6 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 0.72 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.4 Hz, 3H), 1.89-1.96 (m, 1H), 2.02-2.08 (m, 1H), 2.28-2.34 (m, 1H), 2.47 (s, 3H), 3.68-3.70 (m, 1H), 3.75-3.80 (m, 1H), 3.88-3.92 (m, 4H), 4.20-4.39 (m, 5H), 4.40-4.58 (m, 5H), 4.71 (d, J = 10.8 Hz, 1H), 5.10 (d, J = 3.6 Hz, 1H), 6.95 (d, J = 8.8 Hz, 1H), 7.02 (d, J = 7.6 Hz, 1H), 7.07 (s, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.46-7.53 (m, 1H), 7.56-7.67 (m, 4H), 7.70 (d, J = 7.6 Hz, 1H), 7.84 (s, 1H), 8.11-8.14 (m, 1H), 8.36-8.40 (m, 2H), 8.50 (d, J = 6.0 Hz, 1H), 8.58 (d, J = 2.4 Hz, 1H), 8.98 (s, 1H), 9.48 (s, 1H), 12.16-12.29 (m, 1H). |
| 187 |  | C | 924.6 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 0.71 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H), 1.89-2.07 (m, 3H), 2.26-2.39 (m, 2H), 2.46 (s, 3H), 3.64-3.70 (m, 5H), 3.75-3.83 (m, 5H), 4.18-4.23 (m, 2H), 4.27-4.36 (m, 3H), 4.39-4.46 (m, 4H), 4.52-4.57 (m, 1H), 4.69-4.72 (m, 1H), 5.08 (d, J = 4.0 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 7.01 (d, J = 8.0 Hz, 1H), 7.05 (s, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.47-7.51 (m, 1H), 7.55-7.60 (m, 4H), 7.70 (d, J = 8.0 Hz, 1H), 7.80 (s, 1H), 8.09-8.11 (m, 1H), 8.31-8.34 (m, 1H), 8.36-8.39 (m, 1H), 8.45 (d, J = 4.8 Hz, 1H), 8.55 (m, 1H), 8.98 (s, 1H), 9.41 (s, 1H).                       |
| 188 |  | B | 762.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 2.02-2.08 (m, 1H), 2.51-2.78 (m, 6H), 2.85-2.94 (m, 1H), 3.86-3.92 (m, 2H), 4.38-4.40 (m, 2H), 4.45 (s, 2H), 4.98-5.03 (m, 1H), 5.09-5.15 (m, 1H), 5.40-5.45 (m, 1H), 6.88 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.4 Hz, 1H), 7.36-7.40 (m, 3H), 7.47 (d, J = 2.0 Hz, 1H), 7.61-7.67 (m, 2H), 7.82-7.85 (m, 2H), 8.14-8.17 (m, 1H), 8.37 (d, J = 8.0 Hz, 1H), 8.50 (d, J = 6.0 Hz, 1H), 8.58 (d, J = 2.4 Hz, 1H), 9.48 (s, 1H), 11.12 (s, 1H), 12.22 (br, 1H).                                                                                                                                          |

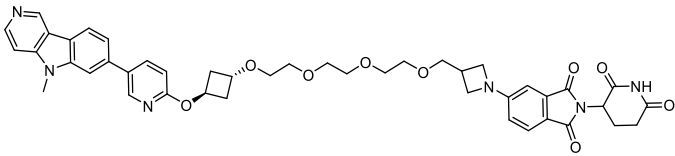
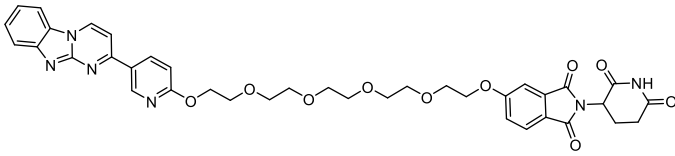
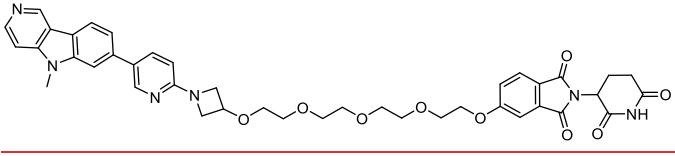
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----|-------------------------------------------------------------------------------------|---|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 189 |    | B | 718.4 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 2.03-2.08 (m, 1H), 2.54-2.70 (m, 6H), 2.84 -2.92 (m, 1H), 4.98-5.03 (m, 1H), 5.10-5.16 (m, 1H), 5.27 (s, 2H), 5.39-5.45 (m, 1H), 6.89 (d, <i>J</i> = 8.8 Hz, 2H), 6.99 (d, <i>J</i> = 8.8 Hz, 1H), 7.40 (d, <i>J</i> = 8.8 Hz, 2H), 7.45-7.47 (m, 1H), 7.57 (d, <i>J</i> = 2.0 Hz, 1H), 7.65-7.70 (m, 2H), 7.86-7.91 (m, 2H), 8.14-8.17 (m, 1H), 8.39 (d, <i>J</i> = 8.0 Hz, 1H), 8.52 (d, <i>J</i> = 6.4 Hz, 1H), 8.58 (d, <i>J</i> = 2.4 Hz, 1H), 9.52 (s, 1H), 11.12 (s, 1H), 12.37 (s, 1H).                                      |
| 190 |   | C | 773.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.84-1.89 (m, 2H), 1.95-2.03 (m, 3H), 2.31-2.39 (m, 4H), 2.81-2.88 (m, 2H), 3.45-3.55 (m, 12H), 3.68 (m, 2H), 4.10 (s, 3H), 4.24 (m, 1H), 5.00-5.04 (m, 1H), 5.03 (s, 1H), 6.55-6.58 (m, 1H), 6.70 (s, 1H), 6.94-6.97 (m, 1H), 7.56-7.57 (m, 1H), 7.80-7.82 (m, 1H), 8.11-8.23 (m, 3H), 8.48-8.51 (m, 1H), 8.67-8.73 (m, 2H), 9.69 (s, 1H), 11.06 (s, 1H).                                                                                                                                                                           |
| 191 |  | A | 773.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.72-1.78 (m, 2H), 1.95-2.01 (m, 1H), 2.31-2.46 (m, 4H), 2.54-2.67 (m, 2H), 2.82-2.91 (m, 1H), 2.95-3.02 (m, 1H), 3.44-3.52 (m, 8H), 3.58-3.60 (m, 2H), 3.73-3.76 (m, 2H), 3.97 (s, 3H), 4.07 (t, <i>J</i> = 8.0 Hz, 2H), 4.20-4.25 (m, 1H), 5.02-5.06 (m, 1H), 5.29-5.35 (m, 1H), 6.59-6.61 (m, 1H), 6.74-6.75 (m, 1H), 6.93-6.95 (d, <i>J</i> = 8.0 Hz, 1H), 7.58-7.68 (m, 3H), 7.99 (s, 1H), 8.17-8.20 (m, 1H), 8.33 (d, <i>J</i> = 8.0 Hz, 1H), 8.52 (d, <i>J</i> = 8.0 Hz, 1H), 8.63-8.64 (m, 1H), 9.39 (s, 1H), 11.07 (s, 1H). |
| 192 |  | C | 759.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.95-1.99 (m, 1H), 2.08 (s, 1H), 2.31-2.37 (m, 2H), 2.41-2.46 (m, 3H), 2.54-2.58 (m, 1H), 2.83-2.89 (m, 1H), 2.96-3.01 (m, 1H), 3.44-3.46 (m, 1H), 3.53-3.57 (m, 6H), 3.64-3.66 (m, 2H), 3.74-3.78 (m, 2H), 3.95 (s, 3H), 4.08 (t, <i>J</i> = 8.4 Hz, 2H), 4.21-4.23 (m, 1H), 5.01-5.06 (m, 1H), 5.30-5.33 (m, 1H), 6.60 (d, <i>J</i> = 9.6 Hz, 1H), 6.75                                                                                                                                                                            |

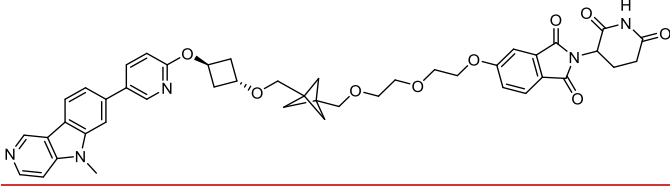
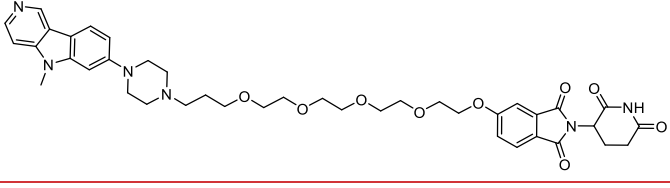
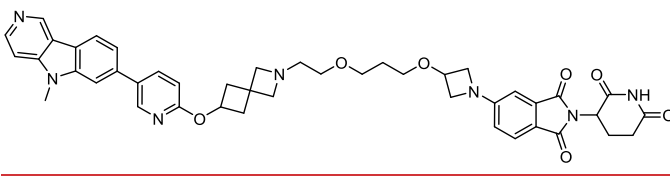
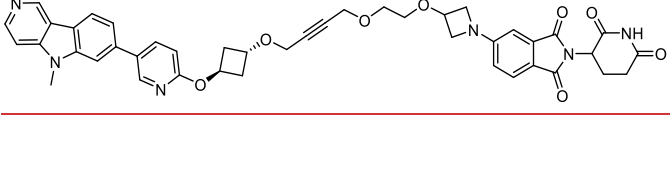
|     |                                                                                                                           |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|-----|---------------------------------------------------------------------------------------------------------------------------|---|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                                                           |   |       | <div> <div>(s, 1H), 6.93 (d, J = 8.4 Hz, 1H), 7.58-7.64 (m, 3H), 7.97 (s, 2H), 8.17-8.20 (m, 1H), 8.31 (d, J = 8.0 Hz, 1H), 8.49 (d, J = 5.6 Hz, 1H), 8.62-8.63 (m, 1H), 9.36 (s, 1H), 11.06 (s, 1H);</div> </div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 193 | <div> <div>  </div> <div></div> </div>   | B | 798.5 | <div> <div>1H NMR: (400 MHz, DMSO-d6)</div> <div> <div>δ: 11.07 (br s, 1H), 9.36 (s, 1H), 8.66 - 8.58 (m, 1H), 8.49 (d, J=5.8 Hz, 1H), 8.32 (d, J=8.2 Hz, 1H), 8.23 (s, 2H), 8.18 (dd, J=2.5, 8.7 Hz, 1H), 7.97 (s, 1H), 7.66 - 7.58 (m, 3H), 6.92 (d, J=8.7 Hz, 1H), 6.81 (br d, J=2.3 Hz, 1H), 6.69 - 6.63 (m, 1H), 5.16 - 5.08 (m, 1H), 5.08 - 5.02 (m, 1H), 4.47 (br s, 1H), 4.30 - 4.22 (m, 3H), 4.19 (s, 1H), 3.99 (s, 1H), 3.95 (s, 3H), 3.95 - 3.89 (m, 4H), 3.86 (br s, 3H), 3.49 - 3.48 (m, 2H), 2.92 - 2.81 (m, 1H), 2.74 (br d, J=6.5 Hz, 2H), 2.58 (br s, 1H), 2.54 (s, 2H), 2.30 - 2.26 (m, 1H), 1.98 (br d, J=4.9 Hz, 1H), 1.85 - 1.74 (m, 2H).</div> </div> </div> |
| 194 | <div> <div>  </div> <div></div> </div> | C | 774.5 | <div> <div>1HNMR (400 MHz, DMSO-d6): δ 1.93-2.11 (m, 2H), 2.54-2.74 (m, 5H), 2.54-2.93 (m, 1H), 3.95-3.98 (m, 2H), 4.31-4.34 (m, 2H), 4.49 (s, 3H), 4.67-4.73 (m, 1H), 5.04-5.14 (m, 2H), 5.41-5.47 (m, 1H), 6.67-6.69 (m, 1H), 6.82-6.83 (m, 1H), 6.99 (d, J = 8.0 Hz, 1H), 7.33-7.36 (m, 1H), 7.53-7.55 (m, 1H), 7.65-7.72 (m, 3H), 7.88 (s, 3H), 8.15-8.18 (m, 1H), 8.25-8.26 (m, 1H), 8.40 (d, J = 8.0 Hz, 1H), 8.52-8.54 (m, 1H), 8.58-8.59 (m, 1H), 9.54 (s, 1H), 11.07 (s, 1H).</div> </div>                                                                                                                                                                                |
| 195 | <div> <div>  </div> <div></div> </div> | A | 786.5 | <div> <div>1H NMR (400 MHz, DMSO-d6): δ 2.01-2.04 (m, 1H), 2.50-2.60 (m, 2H), 2.83-2.92 (m, 1H), 3.52-3.59 (m, 12H), 3.77-3.79 (m, 4H), 4.27-4.28 (m, 5H), 4.43-4.46 (m, 2H), 5.08-5.13 (m, 1H), 6.96 (d, J = 8.4 Hz, 1H), 7.32-7.34 (m, 1H), 7.41 (s, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 8.03 (s, 1H), 8.19-8.22 (m, 1H), 8.35 (d, J = 8.0 Hz, 1H), 8.44 (s, 1H), 8.64-8.65 (m, 1H), 9.22 (s, 1H), 11.10 (s, 1H).</div> </div>                                                                                                                                                                                                                              |

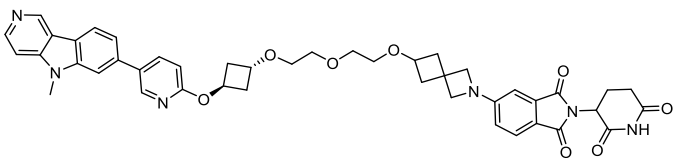
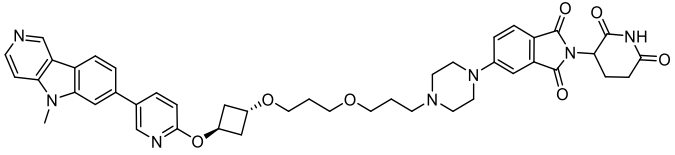
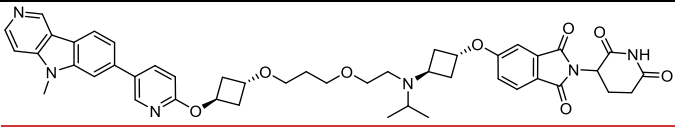
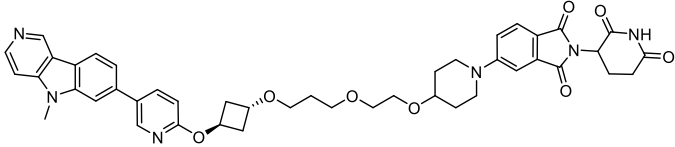
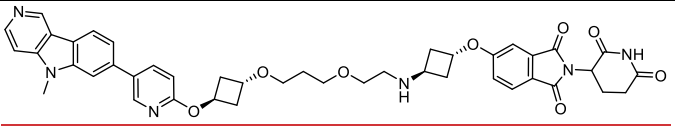
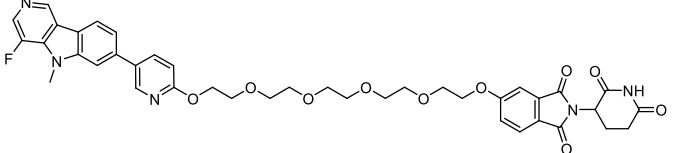
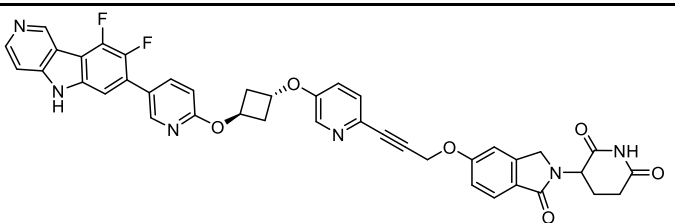
|     |                                                                                                  |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|-----|--------------------------------------------------------------------------------------------------|---|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 196 | <div>  </div>   | C | 968.6 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 0.71 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H), 1.89-2.07 (m, 3H), 2.27-2.35 (m, 2H), 2.46 (s, 3H), 3.57-3.58 (m, 5H), 3.63-3.68 (m, 4H), 3.76-3.81 (m, 5H), 4.17-4.19 (m, 2H), 4.27-4.34 (m, 3H), 4.39-4.46 (m, 4H), 4.52-4.57 (m, 1H), 4.69-4.72 (m, 1H), 5.09 (m, 1H), 6.95 (d, J = 8.8 Hz, 1H), 7.01 (d, J = 8.8 Hz, 1H), 7.04 (s, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.47-7.51 (m, 1H), 7.60-7.64 (m, 4H), 7.70 (d, J = 8.0 Hz, 1H), 7.83 (s, 1H), 8.09-8.14 (m, 1H), 8.34-8.38 (m, 2H), 8.49 (d, J = 4.8 Hz, 1H), 8.55-8.56 (m, 1H), 8.97 (s, 1H), 9.47 (s, 1H).</p> |
| 197 | <div>  </div> | C | 819.5 | <p><sup>1</sup>H NMR: (400 MHz, CDCl<sub>3</sub>) δ: 9.37 (s, 1H), 8.61 (d, J = 6.0 Hz, 1H), 8.51 (d, J = 2.4 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 7.95 - 7.93 (m, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.59 (s, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.4 (d, J = 6.0 Hz, 1H), 6.87 (d, J = 8.0 Hz, 1H), 6.76 (d, J = 2.4 Hz, 1H), 6.50 - 6.48 (m, 1H), 5.44 - 5.41 (m, 1H), 4.96 (dd, J = 5.2, 12.4 Hz, 1H), 4.31 - 4.27 (m, 1H), 4.07 - 4.02 (m, 5H), 3.94 (s, 3H), 3.59 (t, J = 12.4 Hz, 2H), 3.47 (t, J = 6.4 Hz, 2H), 2.92 - 2.78 (m, 3H), 2.65 - 2.48 (m, 6H), 2.32 - 2.27 (m, 2H), 2.19 - 1.99 (m, 4H), 1.86 - 1.79 (m, 1H).</p>        |
| 198 | <div>  </div> | A | 815.5 | <p><sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ 1.46-1.55 (m, 2H), 1.84-1.94 (m, 2H), 2.03-2.07 (m, 1H), 2.35-2.46 (m, 4H), 2.58-2.62 (m, 1H), 2.85-2.94 (m, 3H), 3.50-3.56 (m, 3H), 3.99 (m, 3H), 4.38-4.44 (m, 1H), 5.11-5.16 (m, 1H), 5.28 (s, 2H), 5.31-5.34 (m, 1H), 6.80-6.82 (m, 1H), 6.95-7.01 (m, 3H), 7.18-7.22 (m, 1H), 7.45-7.48 (m, 1H), 7.57-7.58 (m, 1H), 7.66-7.68 (m, 1H), 7.75-7.81 (m, 1H), 7.89-7.91 (m, 1H), 8.03 (s, 1H), 8.19-8.22 (m, 1H), 8.36-8.66 (m, 3H), 9.42 (br, 1H), 11.12 (s, 1H).</p>                                                                                                      |

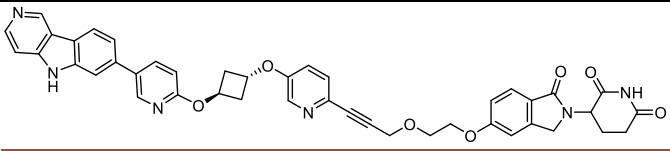
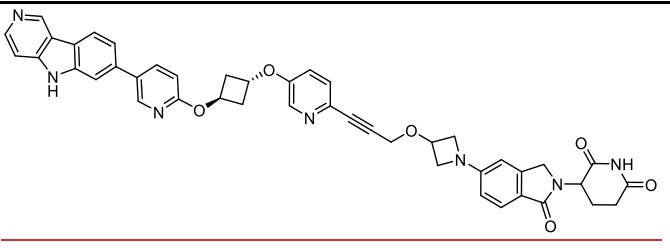
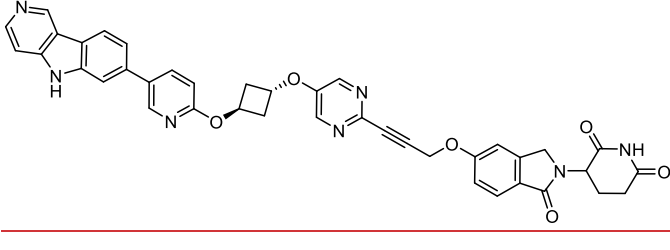
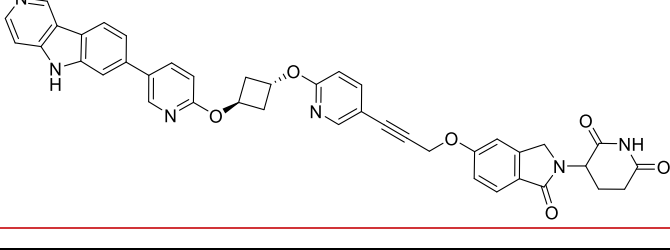
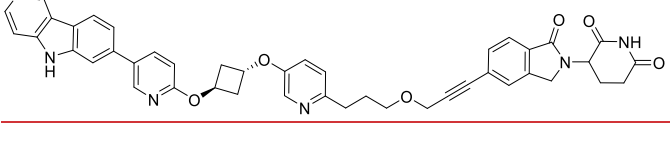
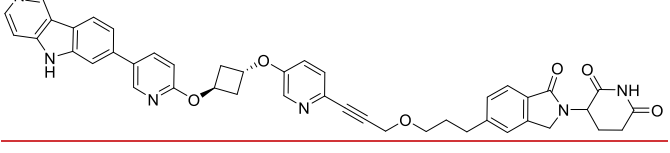
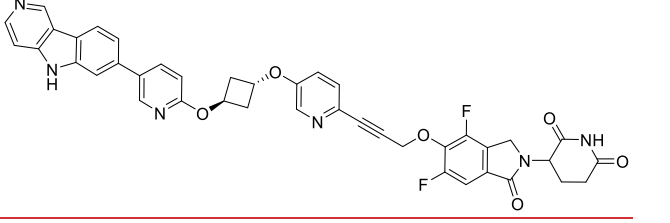
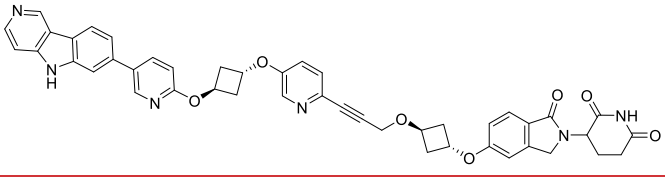
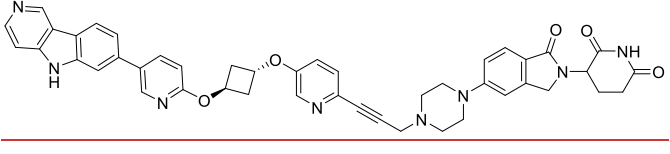
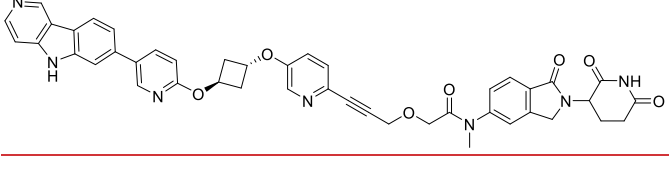
|     |                                                                                     |   |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-----|-------------------------------------------------------------------------------------|---|--------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 199 |    | C | 811.6  | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 1.71-1.98 (m, 6H), 2.06-2.15 (m, 8H), 2.46-2.57 (m, 2H), 2.57-2.88 (m, 4H), 2.96-3.10 (m, 2H), 3.43-3.56 (m, 3H), 3.94 (s, 3H), 4.05-4.20 (m, 2H), 4.91-5.01 (m, 1H), 5.05-5.26 (m, 1H), 5.31-5.42 (m, 1H), 6.82-6.94 (m, 1H), 7.14-7.23 (m, 1H), 7.31-7.45 (m, 2H), 7.48-7.65 (m, 2H), 7.73-7.81 (m, 1H), 7.89-7.99 (m, 1H), 8.19-8.28 (m, 1H), 8.38-8.67 (m, 3H), 9.32-9.42 (m, 1H).                                                                                                                                                          |
| 200 |  | A | 711.6  | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.23 (s, 4H), 1.50-1.54 (m, 4H), 1.97-2.03 (m, 2H), 2.33-2.37 (m, 2H), 2.40-2.46 (m, 2H), 2.54-2.67 (m, 2H), 2.83-2.92 (m, 2H), 3.31 (t, J = 6.4 Hz, 2H), 3.41 (t, J = 6.4 Hz, 2H), 3.82-3.85 (m, 2H), 4.14 (s, 3H), 4.16-4.26 (m, 3H), 4.43-4.48 (m, 1H), 5.03-5.07 (m, 1H), 5.32-5.35 (m, 1H), 6.63-6.66 (m, 1H), 6.78 (s, 1H), 6.98 (d, J = 8.8 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 8.20-8.26 (m, 3H), 8.53 (d, J = 8.4 Hz, 1H), 8.70 (d, J = 2.0 Hz, 1H), 8.76 (d, J = 6.8 Hz, 1H), 9.76 (s, 1H), 11.07 (s, 1H). |
| 201 |  | C | 1012.7 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 0.72 (d, J = 6.4 Hz, 3H), 0.95 (d, J = 6.4 Hz, 3H), 1.89-1.95 (m, 1H), 2.03-2.08 (m, 1H), 2.16-2.35 (m, 2H), 2.46 (s, 3H), 3.52-3.58 (m, 10H), 3.62-3.70 (m, 4H), 3.77-3.78 (m, 5H), 4.14-4.21 (m, 2H), 4.27-4.34 (m, 3H), 4.39-4.47 (m, 4H), 4.52-4.57 (m, 1H), 4.70-4.72 (m, 1H), 5.09-5.10 (m, 1H), 6.95-7.04 (m, 3H), 7.34 (d, J = 8.0 Hz, 1H), 7.47-7.51 (m, 1H), 7.58-7.62 (m, 2H), 7.65-7.73 (m, 3H), 7.87 (s, 1H), 8.11-8.14 (m, 1H), 8.36-8.40 (m, 2H), 8.53 (d, J = 6.4 Hz, 1H), 8.56-8.58 (m, 1H), 8.97 (s, 1H), 9.54 (s, 1H).     |
| 202 |  | B | 800.6  | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.66-1.82 (m, 3H), 1.95-2.00 (m, 1H), 2.28-2.47 (m, 6H), 2.54-2.60 (m, 1H), 2.81-2.91 (m, 4H), 2.97-3.11 (m, 2H), 3.34-3.38 (m, 1H), 3.66-3.69 (m, 2H).                                                                                                                                                                                                                                                                                                                                                                                       |

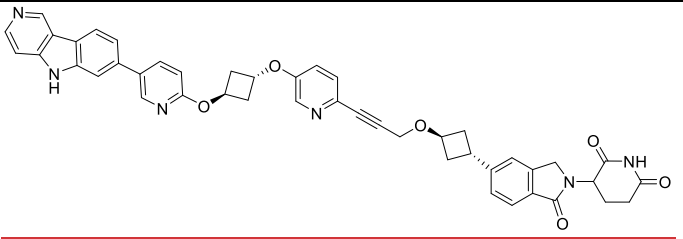
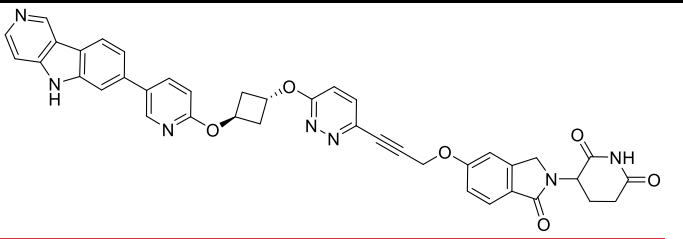
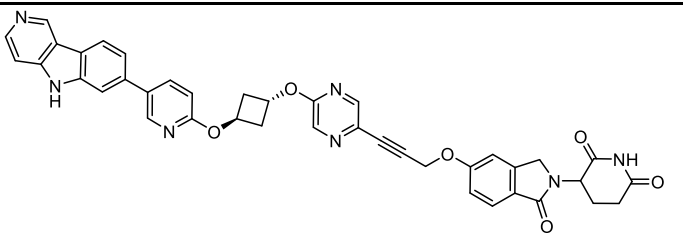
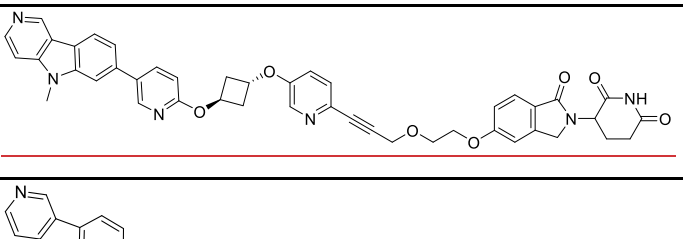
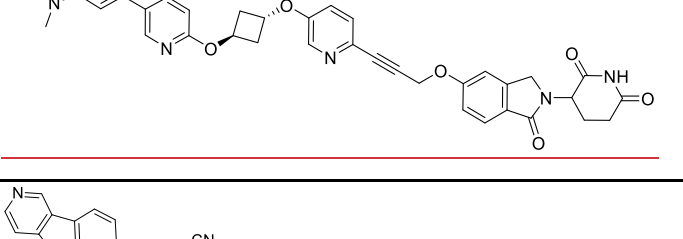
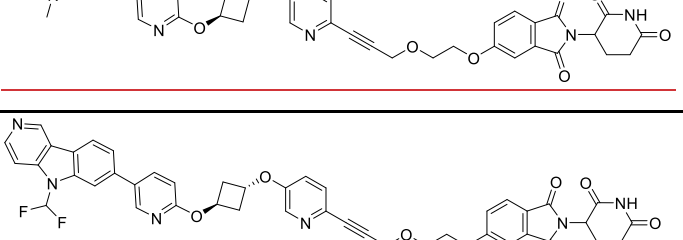
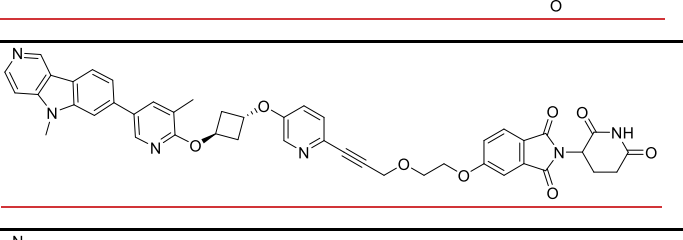
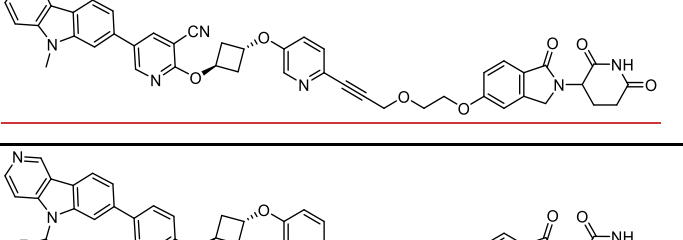
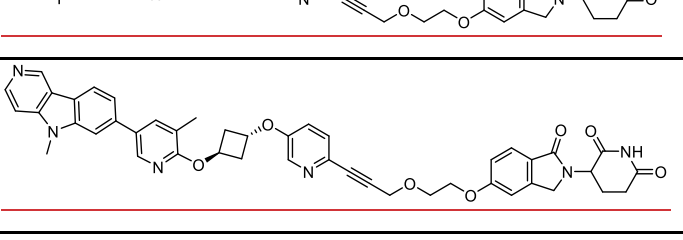
|     |                                                                                                  |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|-----|--------------------------------------------------------------------------------------------------|---|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                                  |   |       | <p>3.78-3.86 (m, 2H), 3.96 (s, 3H), 4.07-4.11 (m, 2H), 4.19-4.23 (m, 3H), 5.00-5.07 (m, 1H), 5.29-5.35 (m, 1H), 6.58-6.64 (m, 1H), 6.73-6.78 (m, 1H), 6.91-6.96 (m, 1H), 7.57-7.67 (m, 3H), 7.95-8.00 (m, 1H), 8.15-8.21 (m, 1H), 8.29-8.35 (m, 1H), 8.48-8.54 (m, 1H), 8.60-8.66 (m, 1H), 9.38 (s, 1H), 11.05 (s, 1H).</p>                                                                                                                                                                                                                                                           |
| 203 | <div>  </div>  | A | 777.5 | <p><sup>1</sup>H NMR: (400MHz, DMSO-d6): δ: 11.13 (s, 1H), 9.37 (s, 1H), 8.96 (d, J = 2.5 Hz, 1H), 8.81 (d, J = 2.5 Hz, 1H), 8.51 (d, J = 5.8 Hz, 1H), 8.35 (d, J = 8.2 Hz, 1H), 8.25 (s, 1H), 8.10 (d, J = 0.9 Hz, 1H), 7.79 (d, J = 8.3 Hz, 1H), 7.74 - 7.67 (m, 1H), 7.63 (d, J = 5.6 Hz, 1H), 7.41 (d, J = 2.1 Hz, 1H), 7.33 (dd, J = 2.3, 8.3 Hz, 1H), 5.19 - 5.04 (m, 1H), 4.60 (dd, J = 3.9, 5.4 Hz, 2H), 4.32 - 4.22 (m, 2H), 3.96 (s, 3H), 3.86 - 3.81 (m, 2H), 3.79 - 3.74 (m, 2H), 3.65 - 3.52 (m, 12H), 2.92 - 2.82 (m, 1H), 2.63 - 2.54 (m, 2H), 2.07 - 1.97 (m, 1H)</p> |
| 204 | <div>  </div> | C | 755.4 | <p><sup>1</sup>H NMR (400 MHz, CDCl3): δ 1.98-2.03 (m, 2H), 2.18-2.22 (m, 2H), 2.69-2.77 (m, 4H), 5.33-5.36 (m, 1H), 5.48-5.52 (m, 1H), 6.86 (d, J = 8.4 Hz, 1H), 7.05 (dd, J = 2.4, 8.4Hz, 1H), 7.22 (d, J = 4.8 Hz, 1H), 7.32 (dd, J = 2.0, 8.4Hz, 1H), 7.37 (d, J = 7.2Hz, 2H), 7.49 (d, J = 1.6 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.8 Hz, 1H), 8.20 (d, J = 2.8 Hz, 1H), 8.35 (s, 1H), 8.57 (d, J = 6.0 Hz, 1H), 9.38 (s, 1H).</p>                                                                                                                                  |
| 205 | <div>  </div> | A | 819.6 | <p><sup>1</sup>H NMR (400 MHz, CD3OD): δ 1.44-1.58 (m, 2H), 1.84-1.91 (m, 2H), 2.04-2.07 (m, 3H), 2.34-2.44 (m, 4H), 2.62-2.93 (m, 7H), 3.46-3.49 (m, 2H), 3.99 (m, 3H), 4.14-4.17 (m, 2H), 4.39-4.42 (m, 1H), 5.11-5.15 (m, 1H), 5.32-5.34 (m, 1H), 6.63-6.64 (m, 1H), 6.75-6.78 (m, 2H), 6.95-6.97 (m, 1H), 7.09-7.13 (m, 1H), 7.36-7.38 (m, 1H), 7.43 (s, 1H), 7.66-7.73 (m, 2H), 7.83-7.85 (m, 1H), 8.02 (s, 1H), 8.20-8.22 (m, 1H), 8.36-8.38 (m, 1H), 8.53-8.55 (m, 1H), 8.66 (s,</p>                                                                                           |

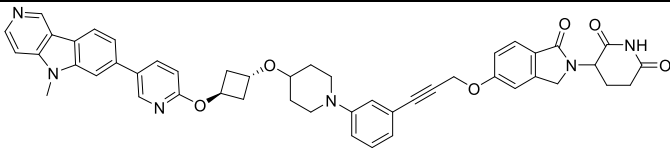
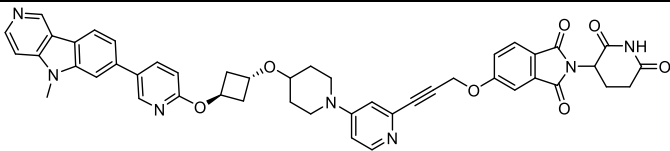
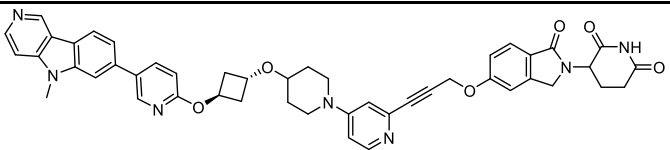
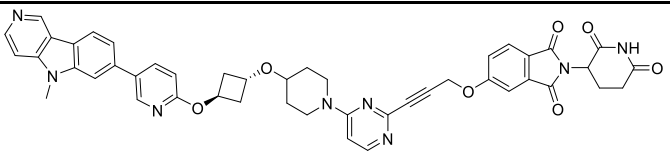
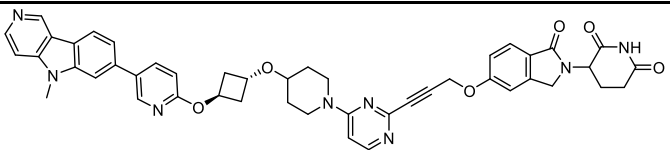
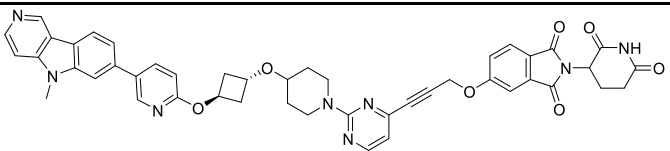
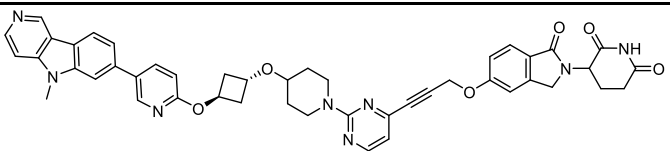
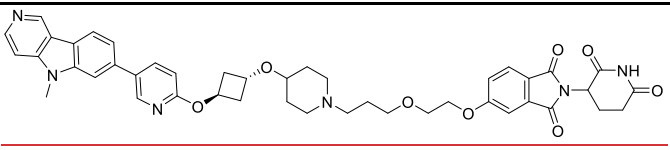
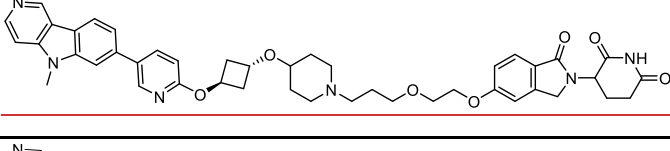
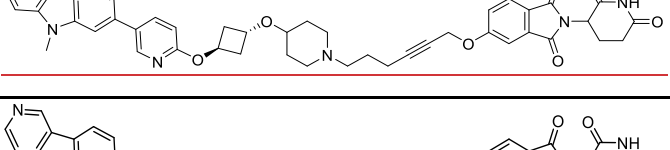
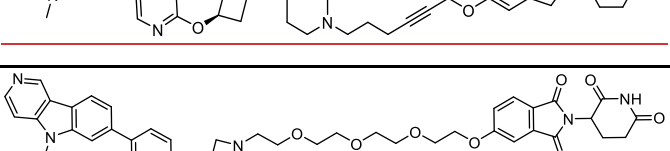
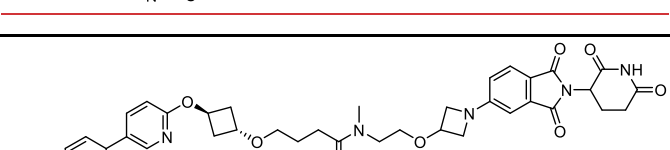
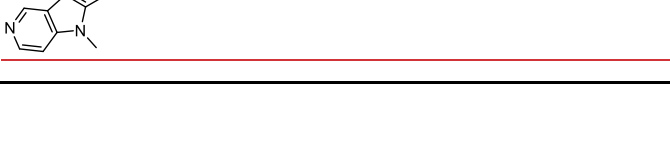
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|------------|--------------------------------------------------------------------------------------------------|----------|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|            |                                                                                                  |          |              | 1H), 9.43 (s, 1H), 11.12 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <u>206</u> | <div>  </div>   | <u>B</u> | <u>803.6</u> | 1HNMR (400 MHz, DMSO-d6): $\delta$ 1.97-2.00 (m, 1H), 2.32-2.37 (m, 2H), 2.42-2.46 (m, 2H), 2.54-2.58 (m, 2H), 2.82-2.91 (m, 1H), 2.95-3.01 (m, 1H), 3.44-3.46 (m, 2H), 3.53-3.56 (m, 10H), 3.62-3.64 (m, 2H), 3.72-3.75 (m, 2H), 4.02 (s, 3H), 4.06 (t, J = 8.0 Hz, 2H), 4.20-4.24 (m, 1H), 5.02-5.06 (m, 1H), 5.29-5.34 (m, 1H), 6.58-6.60 (m, 1H), 6.73-6.75 (m, 1H), 6.95 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.82-7.84 (m, 1H), 8.06 (s, 1H), 8.19-8.22 (m, 1H), 8.39 (d, J = 8.0 Hz, 1H), 8.58-8.59 (m, 1H), 8.65-8.66 (m, 1H), 9.49 (s, 1H), 11.07(s, 1H). |
| <u>207</u> | <div>  </div> | <u>B</u> | <u>739.5</u> | 1H NMR (400 MHz, DMSO-d6): $\delta$ : 11.13 (s, 1H), 9.57 (d, J = 7.2 Hz, 1H), 9.13 (d, J = 2.4 Hz, 1H), 8.63 (dd, J = 2.5, 8.8 Hz, 1H), 8.31 (d, J = 8.2 Hz, 1H), 7.87 - 7.77 (m, 3H), 7.59 - 7.48 (m, 1H), 7.45 - 7.39 (m, 2H), 7.35 (dd, J = 2.3, 8.3 Hz, 1H), 7.05 (d, J = 8.8 Hz, 1H), 5.11 (dd, J = 5.3, 12.8 Hz, 1H), 4.53 - 4.48 (m, 2H), 4.32 - 4.27 (m, 2H), 3.81 - 3.76 (m, 4H), 3.62 - 3.58 (m, 4H), 3.55 (dd, J = 2.8, 5.5 Hz, 4H), 3.52 (s, 4H), 2.94 - 2.84 (m, 1H), 2.65 - 2.54 (m, 2H), 2.09 - 2.00 (m, 1H).                                                                          |
| <u>208</u> | <div>  </div> | <u>A</u> | <u>763.5</u> | 1H NMR (400 MHz, DMSO-d6): $\delta$ 1.99-2.06 (m, 1H), 2.52-2.61 (m, 2H), 2.83-2.92 (m, 1H), 3.52-3.63 (m, 12H), 3.76-3.84 (m, 4H), 3.97 (s, 3H), 4.19-4.23 (m, 2H), 4.26-4.32 (m, 2H), 4.45- .50 (m, 1H), 5.08-5.13 (m, 1H), 6.52 (d, J = 8.8 Hz, 1H), 7.33-7.35 (m, 1H), 7.43 (d, J = 2.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.71 (d, J = 6.0 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.92 (s, 1H), 8.00-8.03 (m, 1H), 8.31 (d, J = 8.4 Hz, 1H), 8.52 (d, J = 6.0 Hz, 1H), 8.58 (d, J = 2.0 Hz, 1H), 9.40 (s, 1H), 11.11 (s, 1H).                                                                         |

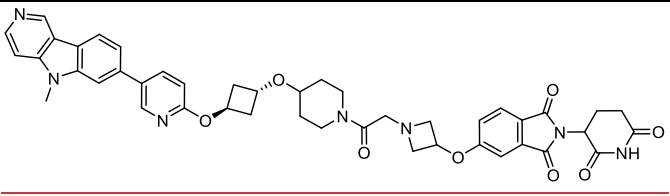
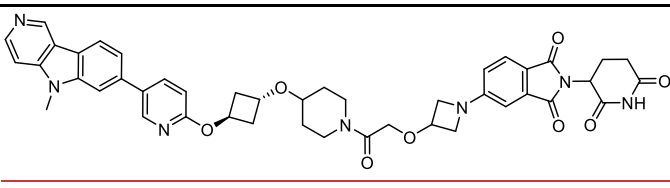
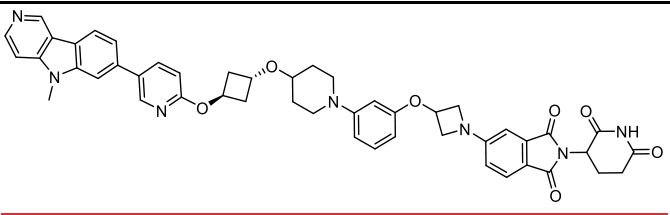
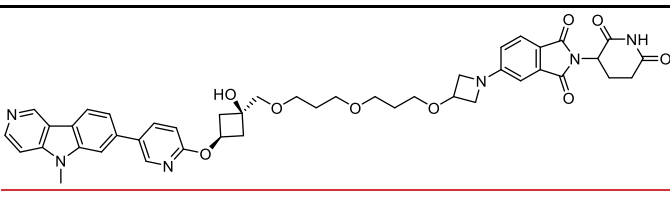
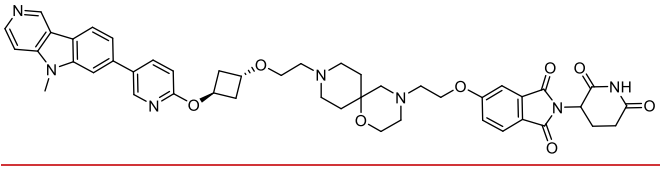
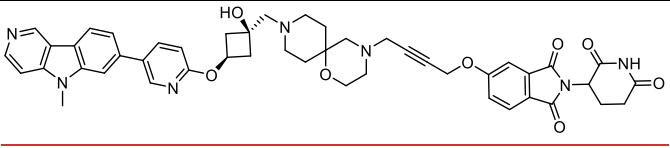
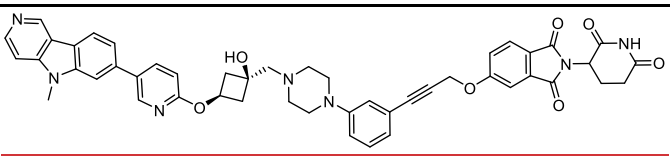
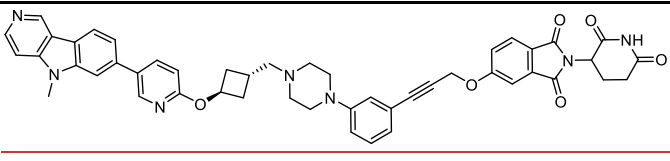
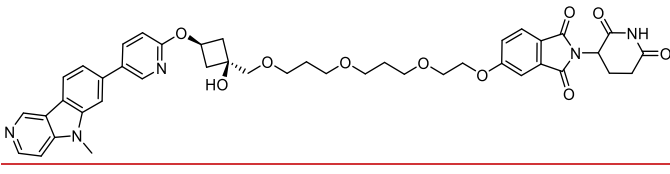
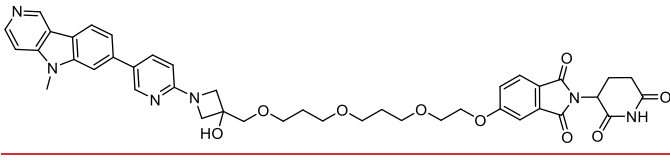
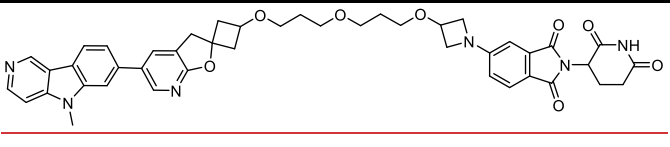
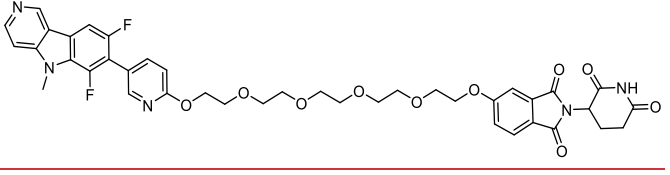
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| 209 |    | <u>A</u> | 800.5 | <p><sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 1.70 (s, 6H), 2.12-2.18 (m, 1H), 2.48-2.59 (m, 4H), 2.76-2.84 (m, 2H), 2.86-2.93 (m, 1H), 3.39 (s, 2H), 3.52 (s, 2H), 3.67-3.69 (m, 2H), 3.72-3.75 (m, 2H), 3.91-3.94 (m, 2H), 4.12 (s, 3H), 4.28-4.36 (m, 4H), 4.93-4.99 (m, 1H), 6.99 (d, J = 8.8 Hz, 1H), 7.19-7.24 (m, 1H), 7.37 (d, J = 2.0 Hz, 1H), 7.70-7.82 (m, 4H), 8.16-8.19 (m, 2H), 8.40 (d, J = 8. Hz, 1H), 8.70-8.72 (m, 2H), 9.61 (s, 1H).</p>                                                                                                             |
| 210 |   | <u>C</u> | 757.6 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ: 15.03 (br s, 1H), 11.18 - 10.95 (m, 2H), 9.55 (s, 1H), 8.64 (br d, J=6.5 Hz, 1H), 8.30 (br d, J=8.3 Hz, 1H), 8.09 (br d, J=6.9 Hz, 1H), 7.81 (br d, J=8.5 Hz, 1H), 7.48 - 7.23 (m, 4H), 5.11 (br dd, J=5.0, 12.7 Hz, 1H), 4.30 (br s, 2H), 4.11 (br d, J=13.1 Hz, 2H), 4.02 (s, 3H), 3.78 (br s, 2H), 3.70 - 3.48 (m, 18H), 3.19 (br s, 3H), 2.96 - 2.82 (m, 1H), 2.62 - 2.55 (m, 3H), 2.04 (br s, 3H).</p>                                                                                                            |
| 211 |  | <u>C</u> | 784.6 | <p><sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ: 9.33 (s, 1H), 8.59 (d, J = 5.6 Hz, 1H), 8.47 (d, J = 2.1 Hz, 1H), 8.21 (d, J = 8.2 Hz, 1H), 7.92 (dd, J = 2.3, 8.3 Hz, 1H), 7.65 (d, J = 8.2 Hz, 1H), 7.55 (s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 6.0 Hz, 1H), 6.86 - 6.77 (m, 2H), 6.55 (br d, J = 6.8 Hz, 1H), 5.17 (quin, J = 6.9 Hz, 1H), 4.93 (dd, J = 5.1, 12.0 Hz, 1H), 4.49 (br s, 1H), 4.25 (br t, J = 7.5 Hz, 2H), 3.96 - 3.84 (m, 5H), 3.57 - 3.35 (m, 10H), 2.93 - 2.66 (m, 7H), 2.39 - 2.27 (m, 2H), 2.16 - 2.08 (m, 1H), 1.93 - 1.82 (m, 2H).</p> |
| 212 |  | <u>A</u> | 769.5 | <p><sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ: 9.39 (s, 1H), 8.61 (d, J=6.0 Hz, 1H), 8.52 - 8.43 (m, 2H), 8.32 - 8.04 (m, 2H), 7.93 (dd, J=2.6, 8.6 Hz, 1H), 7.63 (d, J=8.3 Hz, 1H), 7.59 (s, 1H), 7.53 (dd, J=1.4, 8.1 Hz, 1H), 7.42 (d, J=6.0 Hz, 1H), 6.85 (d, J=8.5 Hz, 1H), 6.78 (d, J=2.0 Hz, 1H), 6.52 (dd, J=2.1, 8.3 Hz, 1H), 5.46</p>                                                                                                                                                                                                                         |

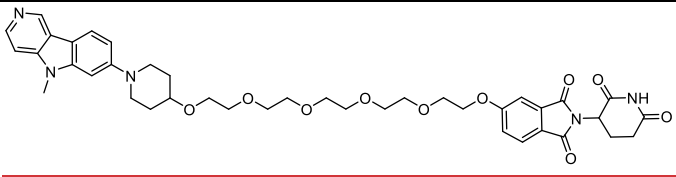
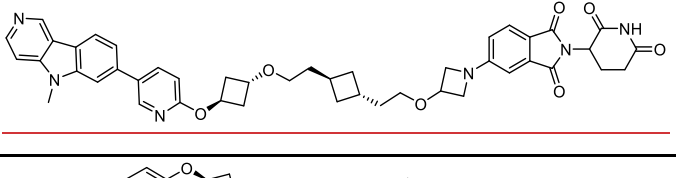
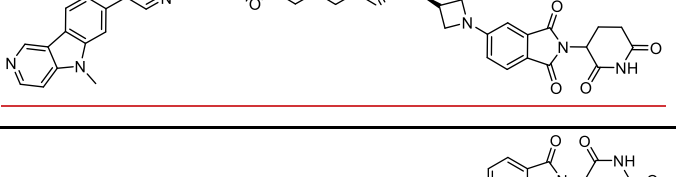
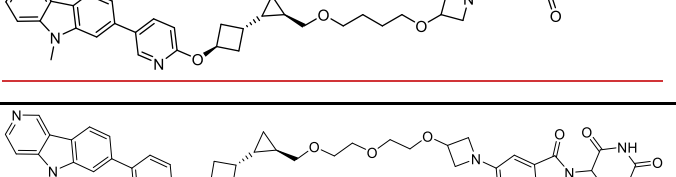
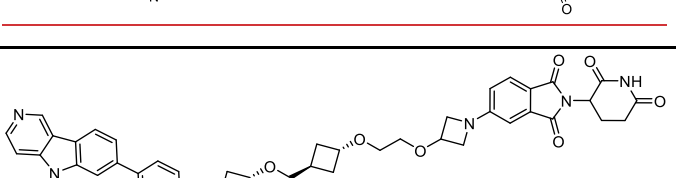
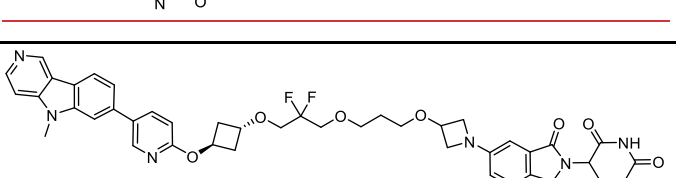
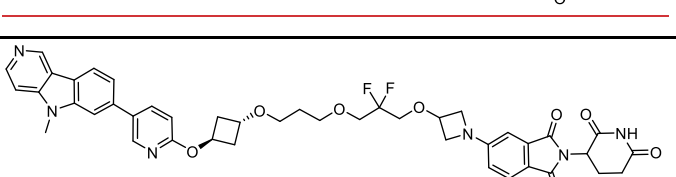
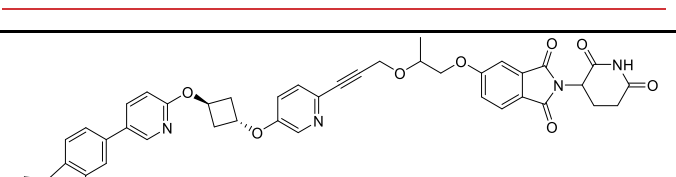
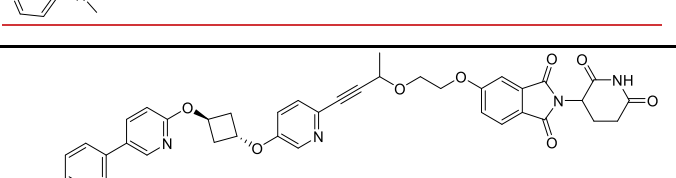
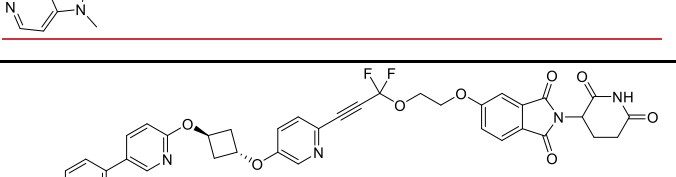
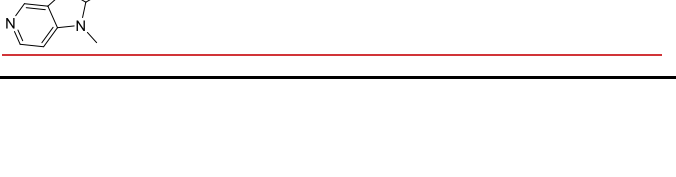
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|     |                                                                                     |   |       | - 5.35 (m, 1H), 4.93 (dd, J=5.2, 12.4 Hz, 1H), 4.61 - 4.43 (m, 2H), 4.29 - 4.27 (m, 2H), 4.27 - 4.21 (m, 2H), 4.20 - 4.16 (m, 2H), 4.00 - 3.89 (m, 5H), 3.78 - 3.63 (m, 4H), 2.92 - 2.67 (m, 3H), 2.64 - 2.55 (m, 2H), 2.51 (td, J=3.5, 7.0 Hz, 2H), 2.16 - 2.08 (m, 1H).                                                                                                                                                                                                                                                                                                                                                                                |
| 213 |   | C | 785.5 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ: 9.38 (s, 1H), 8.59 (d, J = 5.9 Hz, 1H), 8.48 (d, J = 2.3 Hz, 2H), 8.22 (d, J = 8.0 Hz, 1H), 7.92 (dd, J = 2.6, 8.5 Hz, 1H), 7.61 - 7.55 (m, 2H), 7.49 (dd, J = 1.3, 8.1 Hz, 1H), 7.40 (d, J = 6.0 Hz, 1H), 6.85 (d, J = 8.5 Hz, 1H), 6.72 (d, J = 2.0 Hz, 1H), 6.45 (dd, J = 2.1, 8.3 Hz, 1H), 5.47 - 5.35 (m, 1H), 4.92 (dd, J = 5.3, 12.2 Hz, 1H), 4.39 - 4.27 (m, 1H), 4.07 - 3.95 (m, 5H), 3.93 (s, 3H), 3.72 - 3.64 (m, 4H), 3.57 (ddd, J = 3.7, 5.8, 11.9 Hz, 4H), 2.91 - 2.76 (m, 3H), 2.59 (ddd, J = 4.0, 6.9, 13.4 Hz, 4H), 2.52 - 2.43 (m, 2H), 2.32 - 2.23 (m, 2H), 2.16 - 2.07 (m, 1H). |
| 214 |  |   | 786.6 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 215 |  |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
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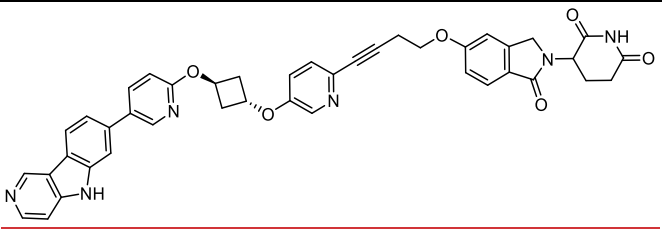
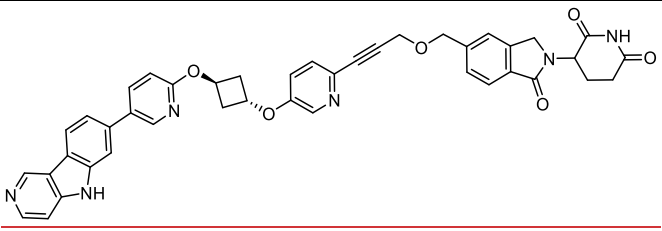
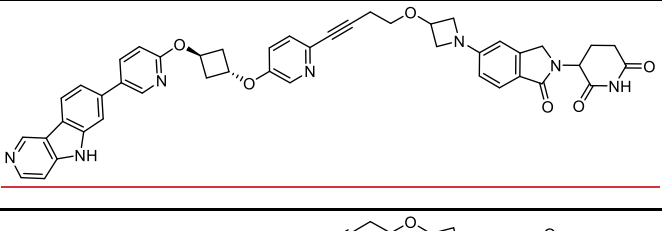
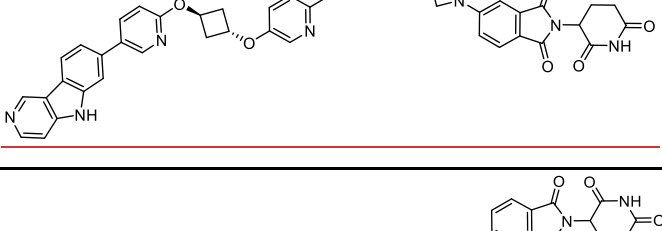
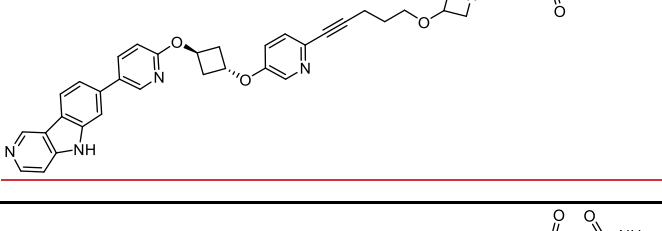
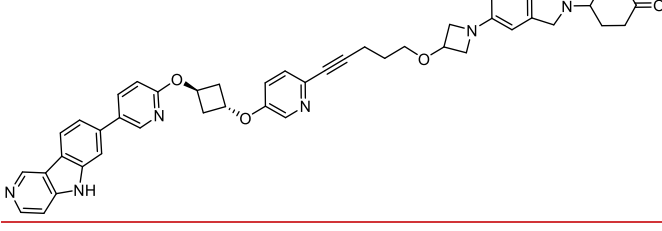
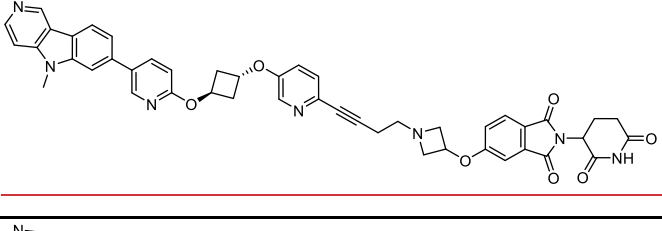
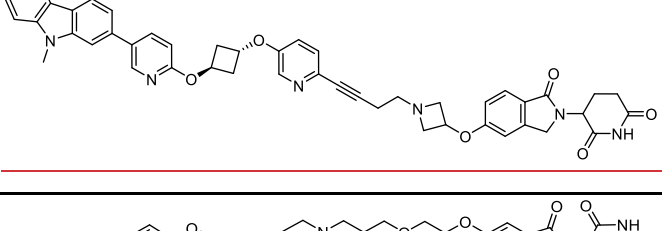
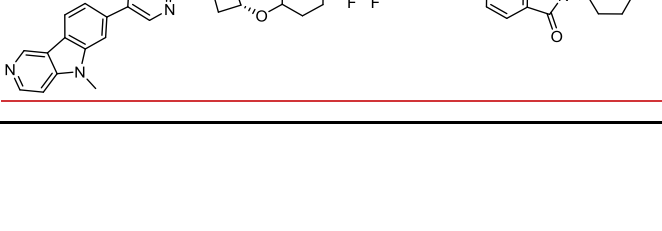
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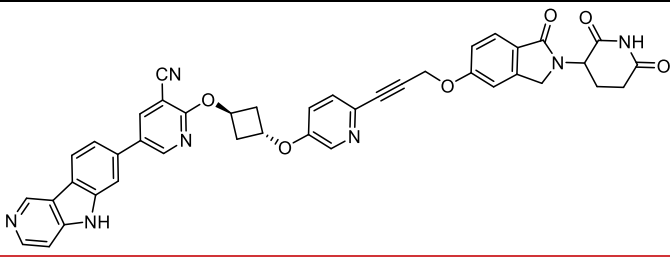
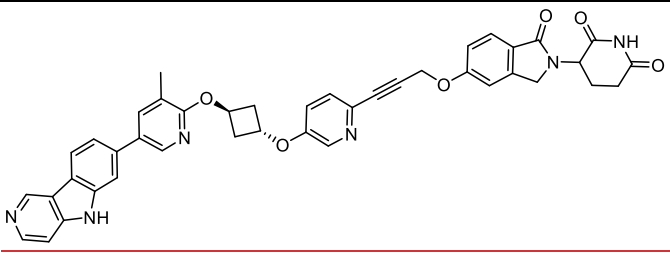
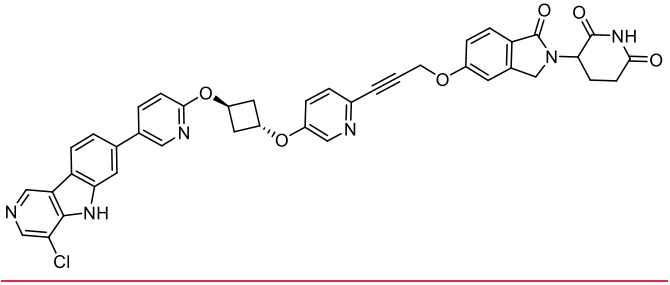
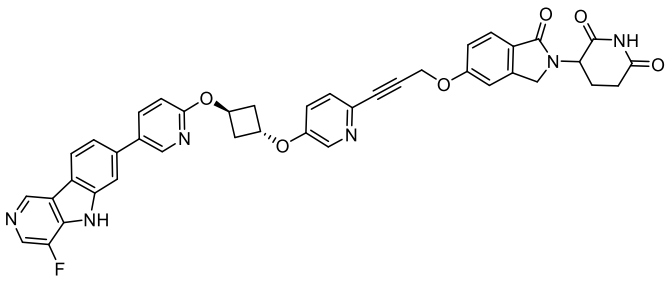
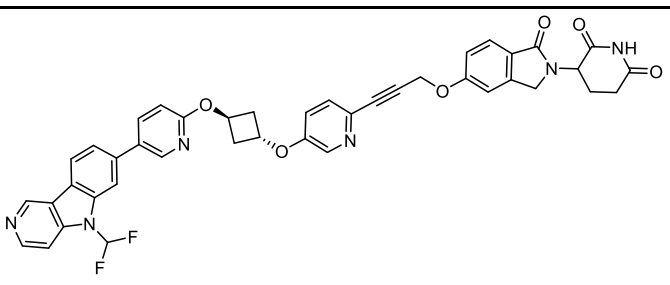
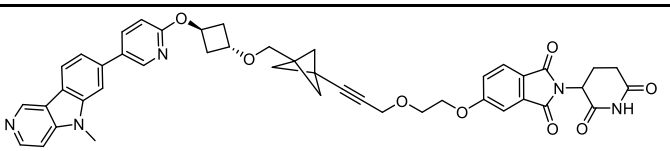
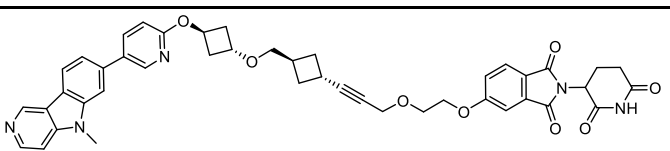
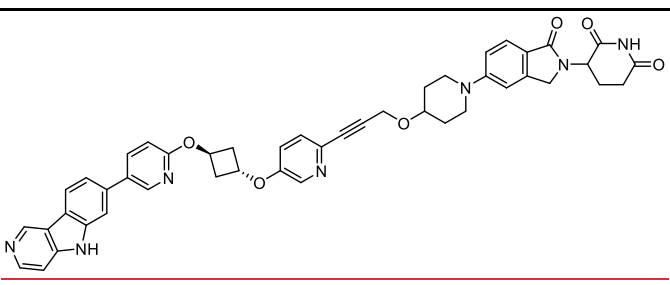
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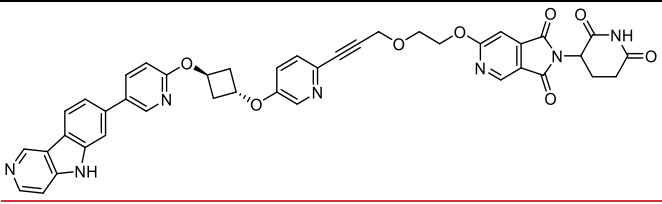
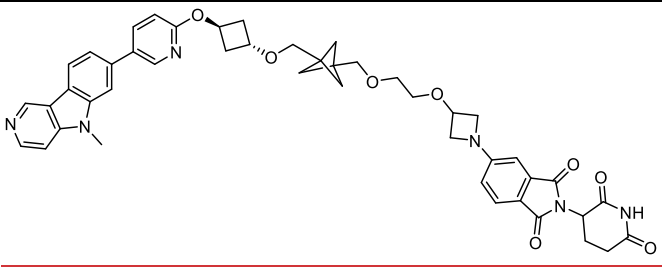
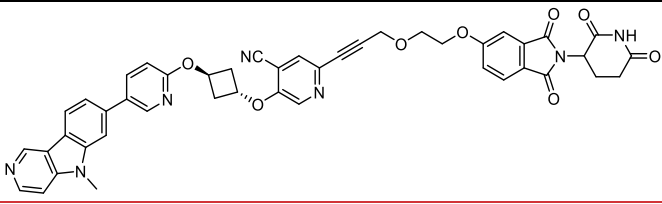
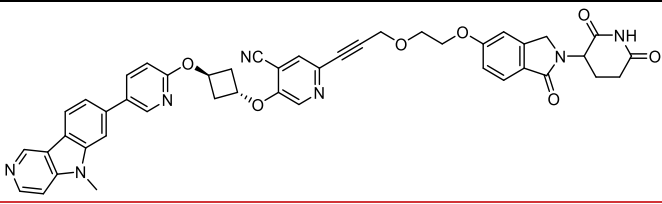
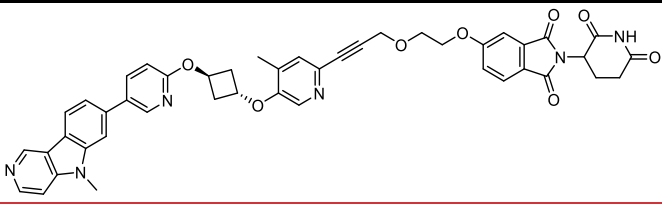
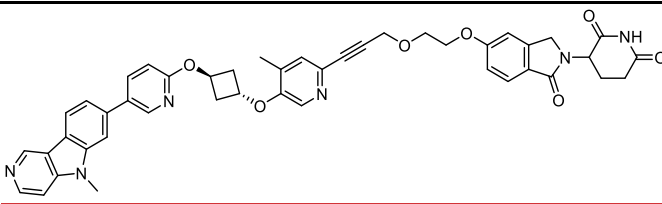
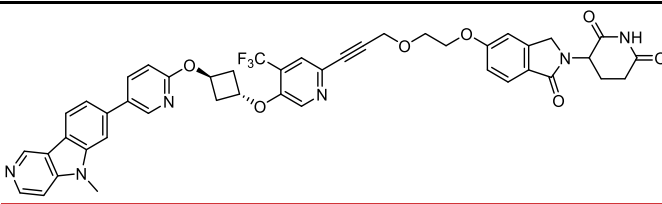
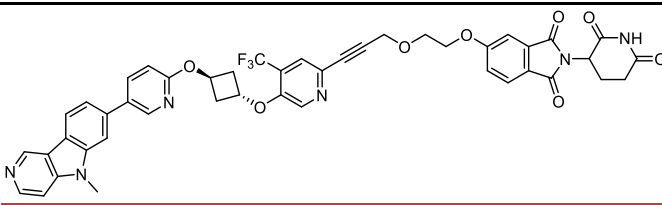
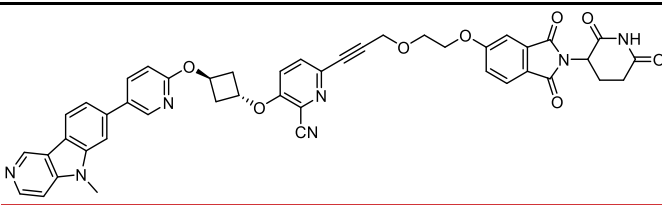
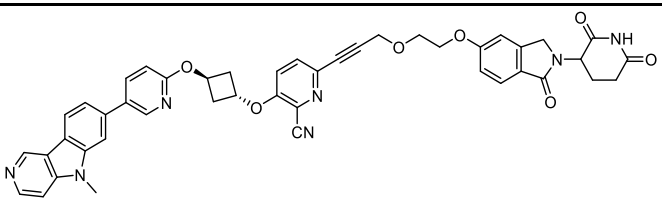
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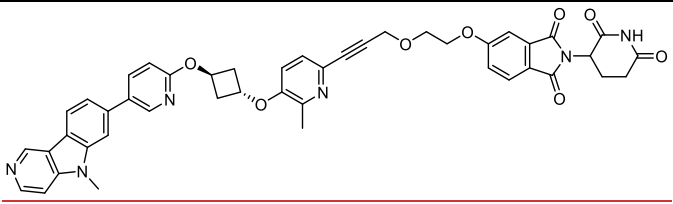
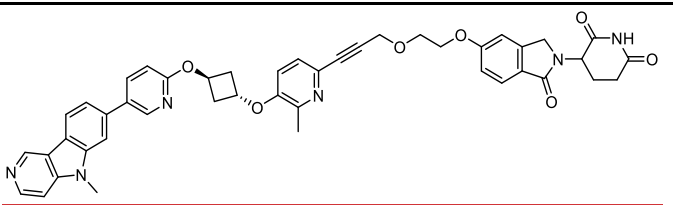
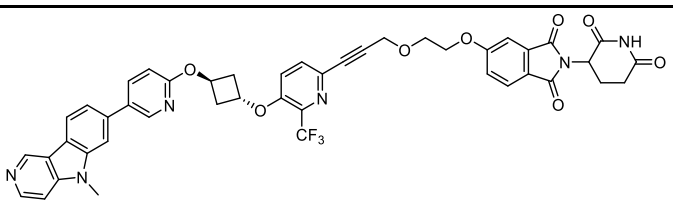
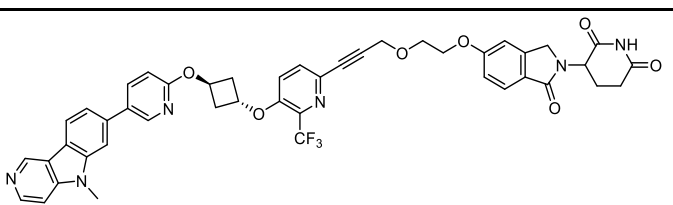
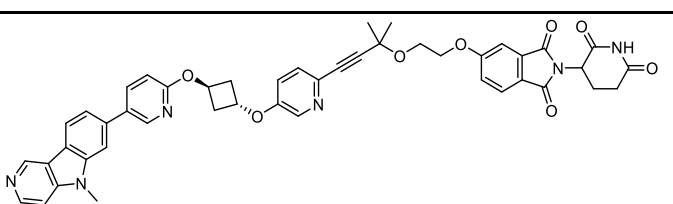
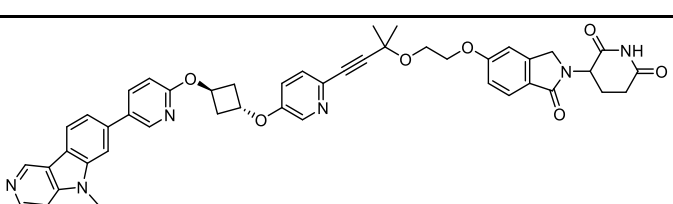
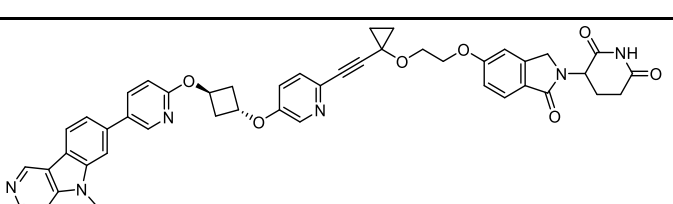
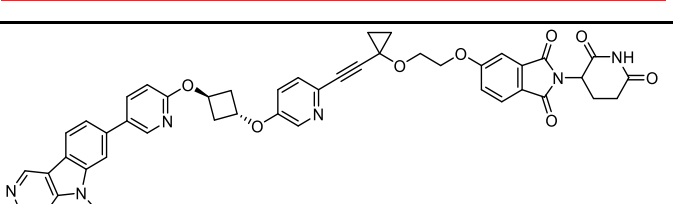
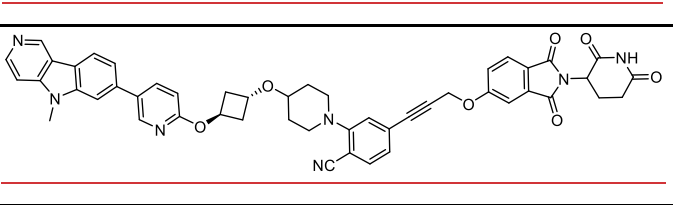
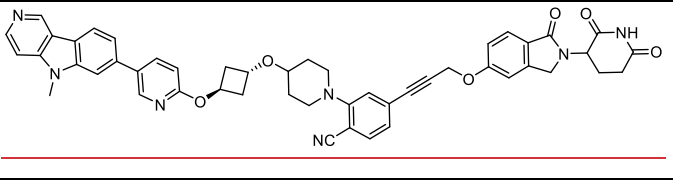
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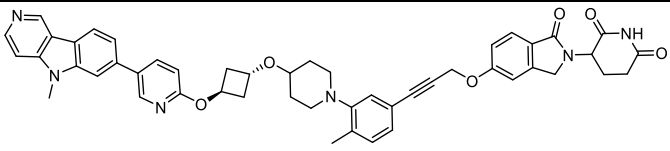
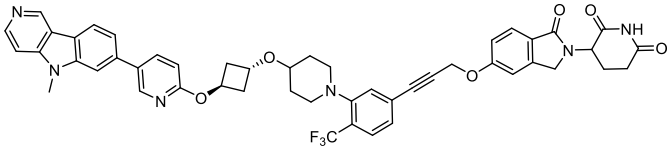
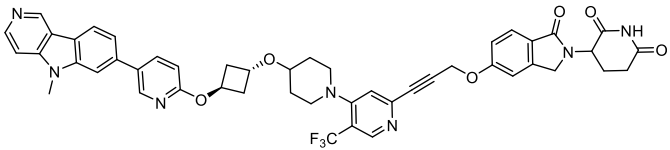
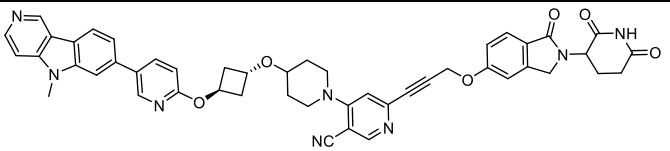
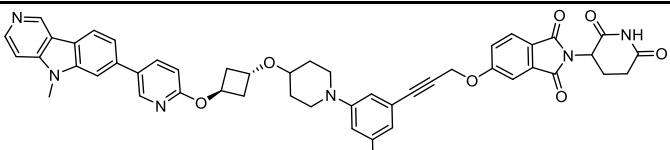
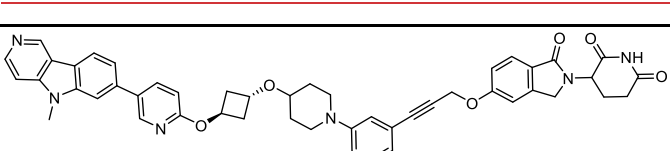
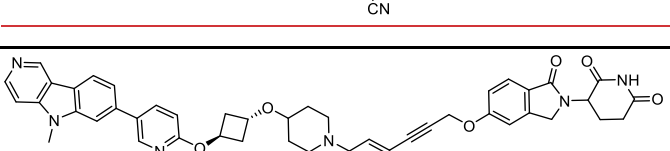
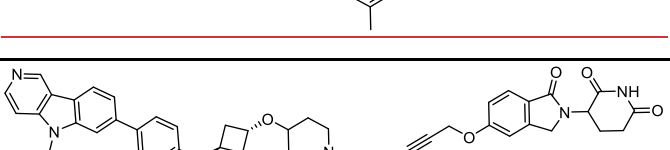
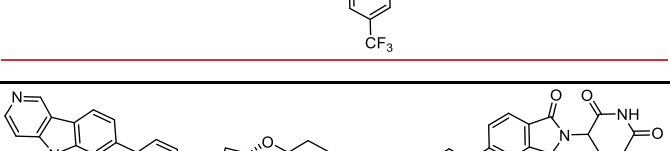
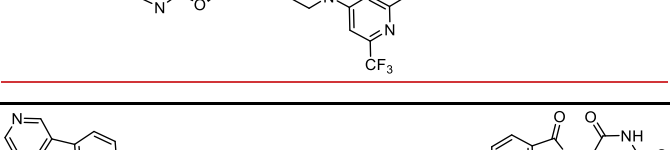
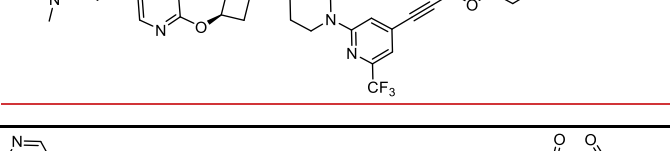
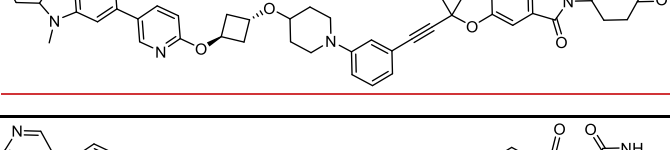
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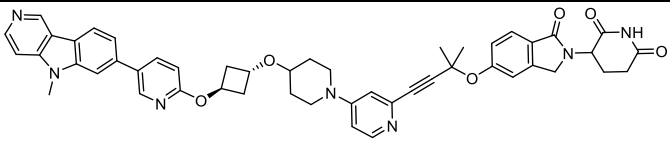
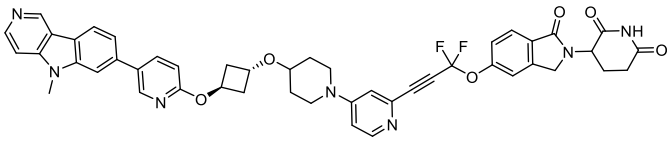
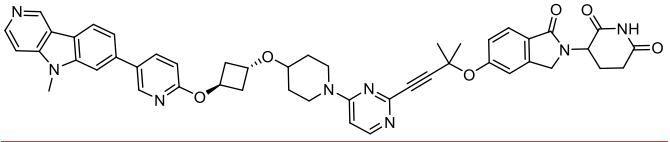
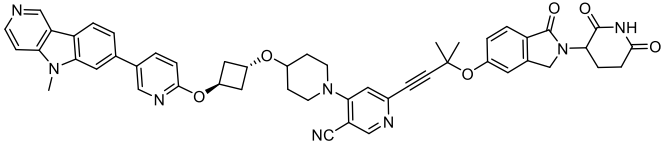
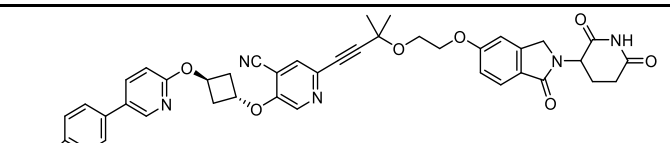
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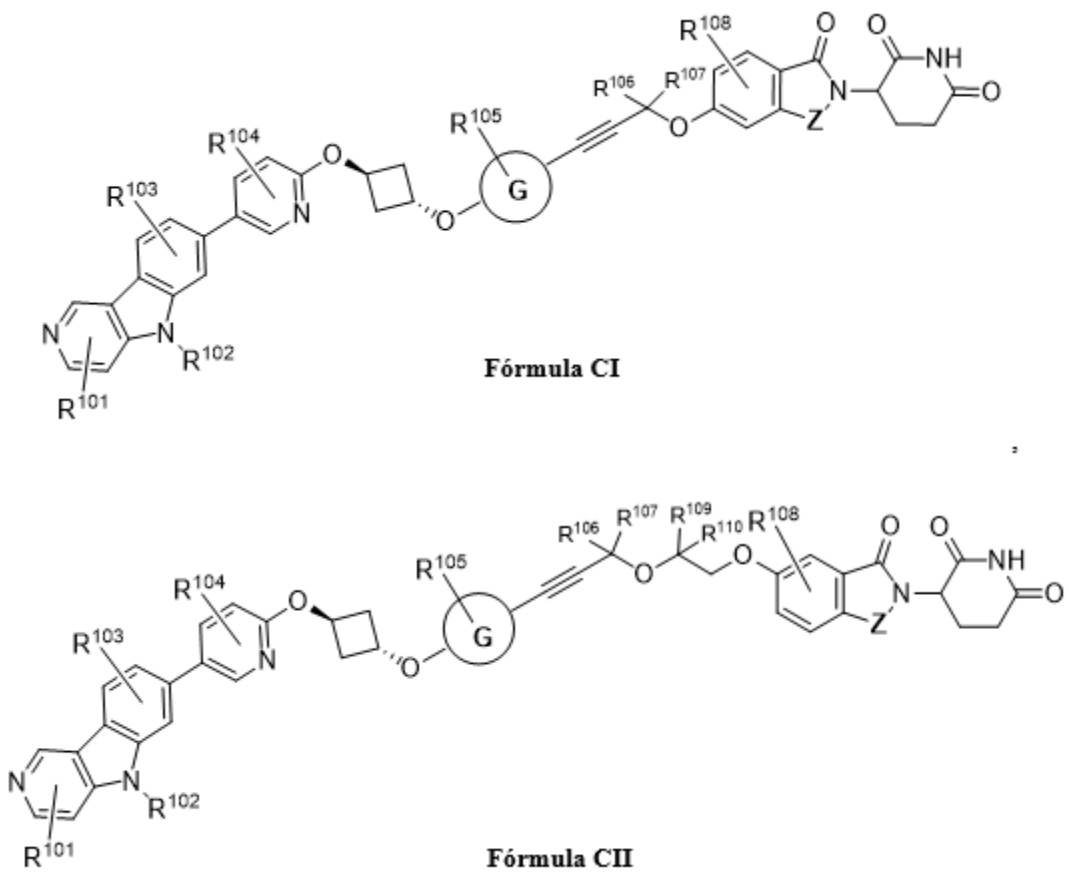
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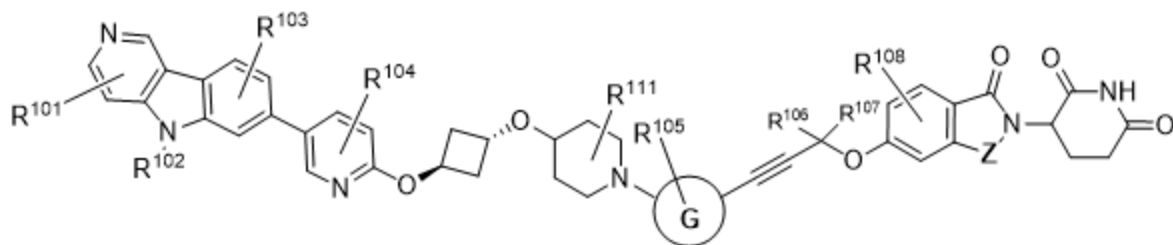
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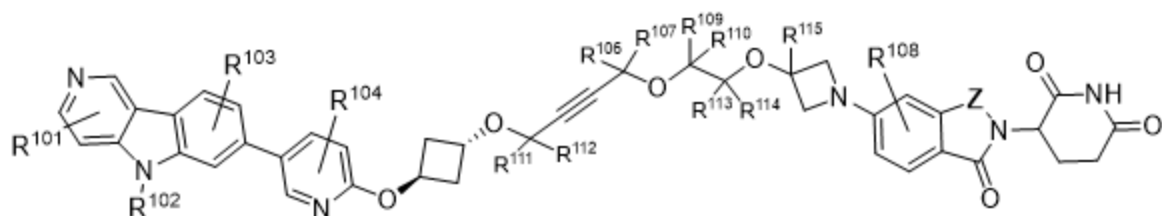
2813. El compuesto de conformidad con cualquiera de las reivindicaciones 1-27 a 12, en donde el compuesto tiene una estructura química seleccionada de las Fórmulas CI hasta CV:



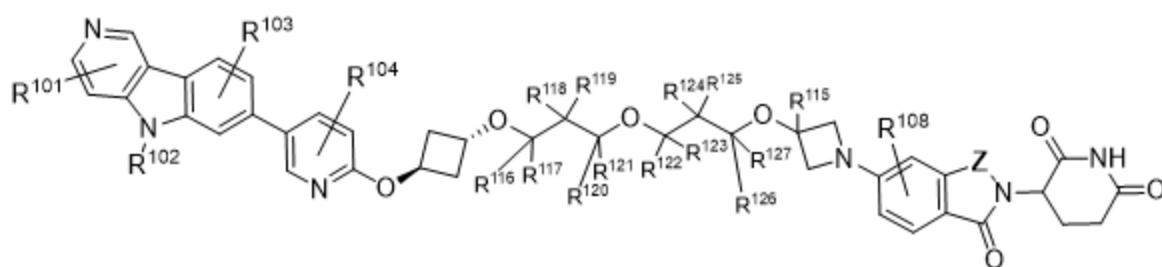
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**Fórmula CIII**



**Fórmula CIV**



**Fórmula CV**

en donde:

$R^{101}$  es 1–2 sustituyentes independientemente seleccionados de H, alquilo de C<sub>1-6</sub>, halógeno, haloalquilo de C<sub>1-6</sub> o ciano;

$R^{102}$  se selecciona de H, alquilo de C<sub>1-6</sub>, o haloalquilo de C<sub>1-6</sub>, ~~cicloalquilo o heterocicloalquilo~~;

$R^{103}$  es 1–2 sustituyentes independientemente seleccionados de H, alquilo de C<sub>1-6</sub>, halógeno, haloalquilo de C<sub>1-6</sub> o ciano;

$R^{104}$  es 1–2 sustituyentes independientemente seleccionados de H, alquilo de C<sub>1-6</sub>, halógeno, haloalquilo de C<sub>1-6</sub> o ciano;

$R^{105}$  es 1–2 sustituyentes independientemente seleccionados de H, alquilo de C<sub>1-6</sub>, halógeno, haloalquilo de C<sub>1-6</sub> o ciano;

$R^{106}$ ,  $R^{107}$ ,  $R^{109}$ ,  $R^{110}$ ,  $R^{111}$ ,  $R^{112}$ ,  $R^{113}$ ,  $R^{114}$ ,  $R^{116}$ ,  $R^{117}$ ,  $R^{120}$ ,  $R^{121}$ ,  $R^{126}$ ,  $R^{127}$ ,  $R^{122}$  y  $R^{123}$  se seleccionan cada uno independientemente de H, alquilo de C<sub>1-6</sub>, halógeno o haloalquilo de C<sub>1-6</sub>;

$R^{108}$  es 1–2 sustituyentes independientemente seleccionados de H, ~~alquilo~~, halógeno, ~~haloalquilo~~, ciano o metoxi;

$R^{115}$  ~~se selecciona de~~ H, ~~alquilo y haloalquilo~~;

$R^{118}$  y  $R^{119}$  se seleccionan independientemente de H, ~~alquilo~~, o halógeno ~~o haloalquilo~~, o  $R^{118}$  y  $R^{119}$  tomados juntos con el átomo de carbono al que se unen representan un anillo cicloalquilo o heterocicloalquilo de 3–6 miembros, tal como ciclopropano o un oxetano;

$R^{124}$  y  $R^{125}$  se seleccionan independientemente de H, ~~alquilo~~, o halógeno ~~o haloalquilo~~,  
o  $R^{124}$  y  $R^{125}$  tomados juntos con el átomo de carbono al que se unen representan  
un anillo cicloalquilo o heterocicloalquilo de 3–6 miembros, tal como ciclopropano  
o un oxetano;

G es un fenilo o un anillo heteroarilo de 5 o 6 miembros; y

Z es  $CH_2$  o  $C=O$ .

**2914.** Una composición que comprende un compuesto bifuncional de conformidad con  
cualquiera de las reivindicaciones 1-~~28~~ a 13, y un vehículo aceptable farmacéuticamente.

~~30. La composición de conformidad con la reivindicación 29, en donde la composición  
comprende, además, al menos uno de un agente bioactivo adicional, otro compuesto  
bifuncional de conformidad con cualquiera de las reivindicaciones 1-29, o una de sus  
combinaciones.~~

~~31. La composición de conformidad con la reivindicación 30, en donde el agente bioactivo  
adicional es un agente anti-neurodegenerativo.~~

~~32. La composición de conformidad con la reivindicación 30, en donde el agente bioactivo  
adicional es un inhibidor de P-gp.~~

~~33. La composición de conformidad con la reivindicación 32, en donde el inhibidor de P-gp es  
Amiodarona, Azitromicina, Captopril, Claritromicina, Ciclosporina, Piperina, Quercetin,  
Quinidina, Quinina, Reserpina, Ritonavir, Tariquidar, Elacridar o Verapamil.~~

~~34. Una composición que comprende un vehículo aceptable farmacéuticamente y una cantidad  
eficaz de al menos un compuesto de conformidad con cualquiera de las reivindicaciones 1-  
28 para usar en un método con el propósito de tratar una enfermedad o trastorno relacionado  
con la proteína Tau en un sujeto, el método comprende administrar la composición a un  
sujeto que lo necesite, en donde el compuesto produce la degradación de la proteína Tau, de  
esta manera se trata o alivia al menos un síntoma de la enfermedad o trastorno.~~

~~35. La composición de conformidad con la reivindicación 34, en donde la enfermedad o  
trastorno se asocia con la acumulación y agregación de Tau.~~

~~36. La composición de conformidad con la reivindicación 34 o 35, en donde la enfermedad o  
trastorno es una enfermedad neurodegenerativa asociada con la acumulación y agregación  
de Tau.~~

~~37. La composición de conformidad con cualquiera de las reivindicaciones 35-36, en donde la  
enfermedad o trastorno es Afasia Epileptiforme Adquirida, Encefalomielitis aguda  
diseminada, ADHD, pupila de Adie, Síndrome de Adie, Adrenoleucodistrofia, Agenesia del~~

~~Cuerpo Calloso, Agnosia, Síndrome de Aicardi, Complicaciones neurológicas del SIDA, Enfermedad de Alexander, Enfermedad de Alper, Hemiplejia alternante, Enfermedad de Alzheimer, Esclerosis Lateral Amiotrófica, Anencefalia, Aneurisma, Síndrome de Angelman, Angiomatosis, Anoxia, Afasia, Apraxia, Quistes Aracnoides, Aracnoiditis, Malformación de Arnold-Chiari, Malformación Arteriovenosa, Síndrome de Asperger, Ataxia, Ataxia Telangiectásica, Ataxias y degeneración espino-cerebelar, Trastorno de hiperactividad y déficit de atención, Autismo, Disfunción Autonómica, Dolor de espalda, Síndrome de Barth, Enfermedad de Batten, Miotonía de Becker, Enfermedad de Behcet, Parálisis de Bell, Blefaroespasma Esencial Benigno, Amiotrofia Focal Benigna, Hipertensión Intracraneana Benigna, Síndrome de Bernhardt-Roth, Enfermedad de Binswanger, Blefaroespasma, Síndrome de Bloch-Sulzberger, Lesiones de nacimiento del plexo braquial, Lesiones del plexo braquial, Síndrome de Bradbury-Eggleston, Tumores de Cerebro y Médula Espinal, Aneurismas de Cerebro, Lesiones del Cerebro, Síndrome de Brown-Sequard, Atrofia Muscular Bulboespinal, Enfermedad de Canavan, Síndrome de Túnel Carpiano, Causalgia, Cavernomas, Angioma Cavernoso, Malformación Cavernosa, Síndrome del cordón cervical central, Síndrome del cordón central, Síndrome de Dolor Central, Trastornos Cefálicos, Degeneración Cerebelar, Hipoplasia Cerebelar, Aneurisma Cerebral, Arteriosclerosis Cerebral, Atrofia Cerebral, Beriberi Cerebral, Gigantismo Cerebral, Hipoxia Cerebral, Parálisis Cerebral, Síndrome Cerebro-Óculo-Facio-Esquelético, Enfermedad de Charcot-Marie-Tooth, Malformación de Chiari, Corea, Coreoacantosis, Polineuropatía desmielinizante inflamatoria crónica (CIDP), Intolerancia Ortostática Crónica, Dolor crónico del síndrome de Cockayne tipo II, Síndrome de Lowry del Coffin, COFS, Colpocefalia, Estado Vegetativo Persistente y Coma, Síndrome del Dolor Regional Complejo, Diplegia Congénita Facial, Miastenia Congénita, Miopatía Congénita, Malformaciones Vasculares Cavernosas Congénitas, Degeneración Corticobasal, Arteritis Craneal, Craneosinostosis, Enfermedad de Creutzfeldt-Jakob, Trastornos por Traumas Acumulativos, Síndrome de Cushing, Enfermedad del Cuerpo de Inclusión Citomegálica, Infección por Citomegalovirus, Síndrome de ojos y pies danzantes, Síndrome de Dandy-Walker, Enfermedad de Dawson, Síndrome de Morsier, Estimulación cerebral profunda para la enfermedad de Parkinson, Parálisis de Dejerine-Klumpke, Demencia por infartos múltiples, Demencia Semántica, Demencia Subcortical, Demencia con Cuerpos de Lewy, Ataxia Cerebelar Dentada, Atrofia Dentatorubral, Dermatomiositis, Dispraxia del Desarrollo, Síndrome de Devic, Neuropatía Diabética, Esclerosis Difusa, Disautonomía, Disgrafía, Dislexia, Disfagia, Dispraxia, Disinergia Cerebelosa Mioclónica, Disinergia Cerebelosa Progresiva, Distonías, Epiléptica Infantil Temprana, Encefalopatía, Síndrome de la silla vacía, Encefalitis letárgica, Encefalocele, Encefalopatía, Angiomatosis Encefalotrigeminal, Epilepsia, Parálisis de Erb-Duchenne y Dejerine-Klumpke, Parálisis de Erb, Enfermedad de Fabry, Síndrome de Fahr, Síncope, Disautonomía Familiar, Hemangioma Familiar, Calcificación Idiopática Familiar de Ganglios basales, Parálisis Familiar Periódica, Parálisis Familiar Espástica, Convulsiones Febriles, Síndrome de Fisher, Síndrome Infantil de Floppy, Ataxia de Friedreich, Demencia Frontotemporal, Enfermedad de Gaucher, Síndrome de Gerstmann, Enfermedad de Gerstmann-Straussler-Scheinker,~~

~~Arteritis de Células Gigantes, Enfermedad de Inclusión de Células Gigantes, Leucodistrofia de Células Globoides, Neuralgia Glossofaríngea, Síndrome de Guillain-Barre, Enfermedad de Hallervorden-Spatz, lesiones de la Cabeza, Cefalea Hemicránea Continua, Espasmos Hemifaciales, Hemiplejia Alternante, Neuropatías Hereditarias, Paraplejia Espástica Hereditaria, Heredopatía Atáctica Polineuritiforme, Herpes Zoster, Herpes Zoster Ótico, Síndrome de Hirayama, Síndrome de Holmes-Adie, Holoprosencefalia asociada al HTLV-1, Mielopatía, Enfermedad de Huntington, Hidranencefalia, Hidrocéfalo, Hidrocéfalo con Presión Normal, Hidromelia, Hiperactividad, Hiperkortisolismo, Hipersomnias, Hipertonía, Hipotonía Infantil, Hipoxia, Encefalomielitis Mediada por Respuesta Inmunitaria, Miositis por Cuerpos De Inclusión, Incontinencia Pigmenti, Hipotonía Infantil, Distrofia Neuroaxonal Infantil, Enfermedad Infantil por Almacenamiento de Ácido Fitánico, Enfermedad de Refsum Infantil, Espasmos Infantiles, Miopatía Inflamatoria, Iniencefalia, Lipodistrofia Intestinal, Quistes Intracraneales, Hipertensión Intracraneana, Síndrome de Isaac, Síndrome de Joubert, Síndrome de Kearns-Sayre, Enfermedad de Kennedy, Síndrome de Kinsbourne, Síndrome de Kleine-Levin, Síndrome de Klippel-Feil, Síndrome de Klippel-Trenaunay (KTS), Síndrome de Klüver-Bucy, Síndrome de Korsakoff, Síndrome Amnésico, Enfermedad de Krabbe, Enfermedad de Kugelberg-Welander, Kurú, Síndrome Miasténico de Lambert-Eaton, Síndrome de Landau-Kleffner, Atrapamiento del nervio cutáneo lateral femoral, Síndrome Medular Lateral, Discapacidad de Aprendizaje, Enfermedad de Leigh, Síndrome de Lennox-Gastaut, Síndrome de Lesch-Nyhan, Leucodistrofia, Síndrome de Levine-Critchley, Demencia con Cuerpos de Lewy, Enfermedades por Almacenamiento de Lípidos, Lisencefalia, Síndrome de Enclaustramiento, Enfermedad de Lou Gehrig, Secuelas del Lupus Neurológico, Complicaciones Neurológicas de la Enfermedad de Lyme, Enfermedad Machado-Joseph, Macroencefalia, Manía, Megaloencefalia, Síndrome de Melkersson-Rosenthal, Meningitis, Meningitis y Encefalitis, Enfermedad de Menkes, Meralgia Parestésica, Leucodistrofia Metacromática, Microcefalia, Migraña, Síndrome de Miller-Fisher, Infartos mínimos, Miopatías Mitocondriales, Síndrome de Mobius, Amiotrofía Monomélica, Enfermedad de la Neurona Motora, Enfermedad de Moyamoya, Mucopolisacáridosis, Mucopolisacáridosis, Neuropatía Motora Multifocal, Demencia por Múltiples Infartos, Esclerosis Múltiple, Atrofia de Múltiples Sistemas, Atrofia de Múltiples Sistemas con Hipotensión Ortostática, Distrofia Muscular, Miastenia Congénita, Miastenia Gravis, Esclerosis Mielinoclástica Difusa, Encefalopatía Mioclónica de los Niños, Mioclono, Miopatía, Miopatía Congénita, Miopatía Tirotóxica, Miotonía, Miotonía Congénita, Narcolepsia, Neuroacantosis, Neurodegeneración Cerebral por Acumulación de Hierro, Neurofibromatosis, Síndrome Neuroléptico Maligno, Complicaciones Neurológicas del SIDA, Complicaciones Neurológicas de la Enfermedad de Lyme, Consecuencias Neurológicas de la infección por Citomegalovirus, Manifestaciones Neurológicas de la Enfermedad de Pompe, Secuelas Neurológicas del Lupus, Neuromielitis Óptica, Neuromiotonía, Lipofuscinosis Neuronal Ceroide, Trastornos de la Migración Neuronal, Neuropatía Hereditaria, Neurosarcoidosis, Neurotoxicidad, Nevo Cavernoso, Enfermedad de Niemann-Pick, Hidrocéfalo con Presión Normal, Neuralgia Occipital, Obesidad, Secuela Oculta del Disrafismo Espinal, Síndrome de Ohtahara, Atrofia Olivopontocerebelosa,~~

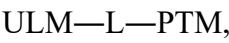
~~Opsoclonus Myoclonus, Hipotensión Ortostática, Síndrome de O'Sullivan-McLeod, Síndrome de Uso Excesivo, Dolor Crónico, Neurodegeneración Asociada a la Pantotenato Quinasa, Síndromes Paraneoplásicos, Parestesias, Enfermedad de Parkinson, Coreoatetosis paroxística, Hemicránea paroxística, Síndrome de Parry-Romberg, Enfermedad de Pelizaeus-Merzbacher, Síndrome de Pena-Shokeir II, Quiste Perineural, Parálisis Periódica, Neuropatía Periférica, Leucomalacia Periventricular, Estado Vegetativo Persistente, Trastornos Profundos del Desarrollo, Enfermedad por Almacenamiento de Ácido Fitánico, Enfermedad de Pick, Síndrome del Nervio Pinzado por el Músculo Piriforme, Tumores de la Pituitaria, Polimiositis, Enfermedad de Pompe, Porencefalia, Neuralgia post-herpética, Encefalitis postinfecciosa, Síndrome post-Polio, Hipotensión Postural, Síndrome de Taquicardia Postural Ortostática, Síndrome de Taquicardia Postural, Atrofia Dentatum Primaria, Esclerosis Lateral Primaria, Afasia Progresiva Primaria, Enfermedad por Priones, Atrofia Hemifacial Progresiva, Ataxia Locomotriz Progresiva, Leucoencefalopatía Multifocal Progresiva, Poliodistrofia Esclerosante Progresiva, Parálisis Supranuclear Progresiva, Prosopagnosia, Pseudotumor Cerebri, Síndrome de Ramsay Hunt (anteriormente conocido como), Síndrome de Ramsay Hunt II (anteriormente conocido como), Encefalitis de Rasmussen, Síndrome de Distrofia Simpática Refleja, Enfermedad de Refsum, Enfermedad de Refsum Infantil, Trastornos de Movimientos Repetitivos, Lesiones por Estrés Repetitivo, Síndrome de Piernas Inquietas, Mielopatías Asociadas a Retrovirus, Síndrome de Rett, Síndrome de Reye, Síndrome de Riley-Day, Quistes en la Raíz del Nervio Sacro, Mal de San Vito, Enfermedad de la Glándula Salival, Enfermedad de Sandhoff, Enfermedad de Schilder, Esquizencefalia, Enfermedad de Seitelberger, Trastornos Convulsivos, Demencia Semántica, Displasia Septo-Óptica, Síndrome del Bebé Sacudido, Síndrome de Shingles-Shy-Drager, Síndrome de Sjogren, Apnea de Sueño, Enfermedad del Sueño, Síndrome de Sotos, Espasticidad, Espina Bífida, Infarto de la Médula Espinal, Lesión de la Médula Espinal, Tumores de la Médula Espinal, Atrofia Muscular Espinal, Atrofia Espinocerebelosa, Degeneración Espinocerebelar, Síndrome de Steele-Richardson-Olszewski, Síndrome de Stiff Person, Degeneración Estriatonigral, Infarto Cerebral, Síndrome de Sturge-Weber, Panencefalitis Esclerosante Subaguda, Encefalopatía Arteriosclerótica Subcortical, Cefalea SUNCT, Trastornos de la Deglución, Corea de Sydenham, Síncope, Esclerosis Espinal Sifilítica, Siringohidromielia, Siringomielia, Lupus Eritematoso Sistémico, Disquinesia Tardía de Tabes Dorsalis, Quistes de Tarlov, Enfermedad de Tay-Sachs, Arteritis Temporal, Síndrome de la Médula Espinal Atada, Miotonía de Thomsen, Síndrome de la Salida Torácica, Miopatía Tirotóxica, Tic Doloroso, Parálisis de Todd, Síndrome de Tourette, Ataque de Isquemia Transitoria, Encefalopatías Espongiformes Transmisibles, Mielitis Transversa, Lesión Cerebral Traumática, Temblor, Neuralgia del Trigémino, Paraparésis Espástica Tropical, Esclerosis Tuberosa, Tumor Vascular Eréctil, Vasculitis que incluyen la Arteritis Temporal, Enfermedad de Von Economo, Enfermedad de Von Hippel-Lindau (VHL), Enfermedad de Von Recklinghausen, Síndrome de Wallenberg, Enfermedad de Werdnig-Hoffman, Síndrome de Wernicke-Korsakoff, Síndrome de West, Latigazo, Enfermedad de Whipple, Síndrome de Williams,~~

~~Enfermedad de Wilson, Atrofia Muscular Espinal y Bulbar Ligada al X, o Síndrome de Zellweger.~~

- ~~38.—La composición de conformidad con cualquiera de las reivindicaciones 33-34, en donde la enfermedad o trastorno es un trastorno neurológico con al menos uno de enfermedad de Huntington, distrofia muscular, enfermedad de Parkinson, enfermedad de Alzheimer, enfermedad de Batten, lesiones de la médula espinal y el cerebro, trastornos convulsivos, epilepsia, tumores cerebrales, meningitis, enfermedades autoinmunitarias tal como la esclerosis múltiple, Neurofibromatosis, Depresión, Esclerosis Lateral Amiotrófica, Malformaciones Arteriovenosas, Aneurisma Cerebral, Fístulas Arteriovenosas de la Duramadre, Cefalea, Trastornos de la Memoria, Neuropatía Periférica, Neuralgia post Herpética, Tumor de la Médula Espinal, e Infarto Cerebral.~~
- ~~39.—La composición de conformidad con cualquiera de las reivindicaciones 35-36, en donde la enfermedad o trastorno es la enfermedad de Alzheimer.~~

REIVINDICACIONES

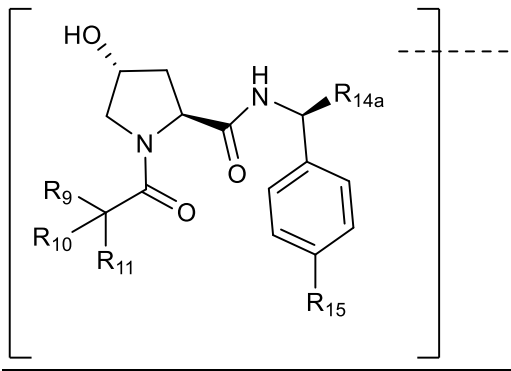
1. Un compuesto bifuncional que tiene la estructura química:



o una de sus sales aceptables farmacéuticamente,

en donde:

la ULM está representada por la estructura:

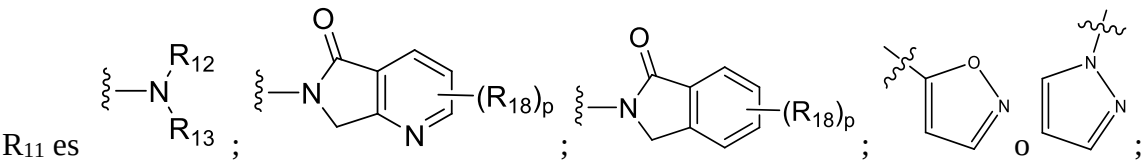


en donde:

es H, C<sub>1-6</sub> alquilo, C<sub>1-6</sub> haloalquilo, C<sub>1-6</sub> alquilo-OH, o ciclopropilo;

R<sub>9</sub> es H;

R<sub>10</sub> es H, etilo, isopropilo, tert-butilo, sec-butilo, ciclopropilo, ciclobutilo, ciclopentilo, o ciclohexilo;



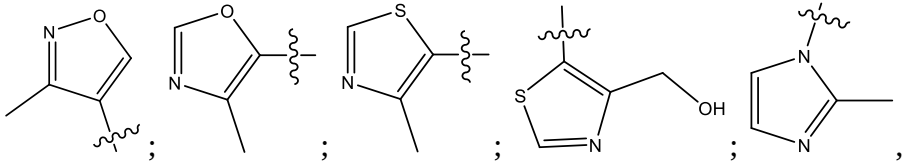
p es 0, 1, 2, 3, o 4;

cada R<sub>18</sub> es independientemente halo, alcoxi, ciano, alquilo, haloalquilo, haloalcoxi;

R<sub>12</sub> es H, C=O;

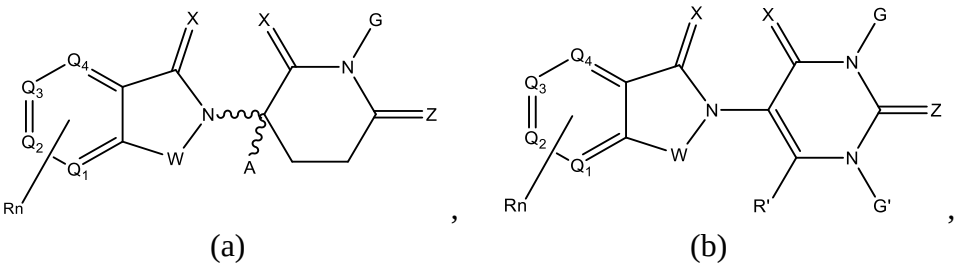
R<sub>13</sub> es H, C<sub>1-6</sub> alquilo, o C<sub>1-6</sub> alquilcarbonilo; y

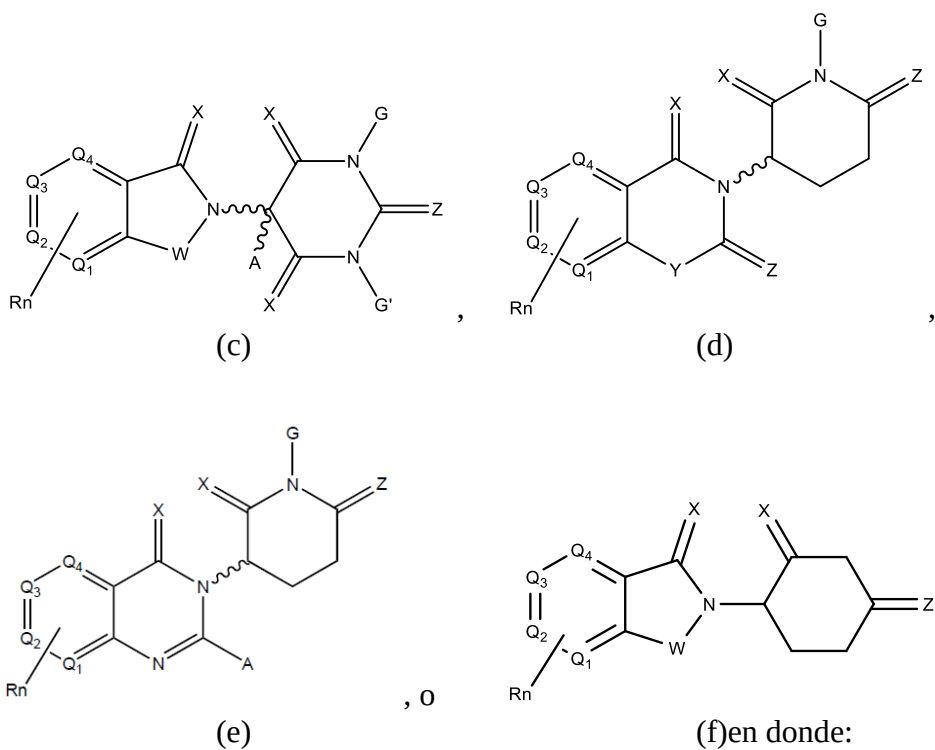
R<sub>15</sub> se selecciona del grupo que consiste en H, halógeno, CN, OH, y NO<sub>2</sub>;



en donde la línea discontinua indica el punto de acoplamiento de una porción de enlazador químico;

o en donde la ULM está representada por la estructura:





W se selecciona del grupo que consiste en CH<sub>2</sub>, CHR, C=O, SO<sub>2</sub>, y NH;

cada X se selecciona independientemente del grupo que consiste en O, S, y H<sub>2</sub>;

Y se selecciona del grupo que consiste en CH<sub>2</sub>, -C=CR', NH, O, y S;

Z se selecciona del grupo que consiste en O, S, y H<sub>2</sub>;

G y G' se seleccionan independientemente del grupo que consiste en H, alquilo, OH, R'OCOOR, R'OCONRR'', y bencilo opcionalmente sustituido con R';

Q<sub>1</sub>, Q<sub>2</sub>, Q<sub>3</sub>, y Q<sub>4</sub> representan un carbono C sustituido con un grupo independientemente seleccionado de R', N o N-óxido;

A se selecciona independientemente del grupo H, Cl y F;

R comprende -CONR'R'', -OR', -NR'R'', -SR', -SO<sub>2</sub>R', -SO<sub>2</sub>NR'R'', -CR'R''-, -CR'NR'R''-, -P(O)(OR')R'', -P(O)R'R'', -OP(O)(OR')R'', -OP(O)R'R'', -Cl, -F, -Br, -I, -CF<sub>3</sub>, -CN, -NR'SO<sub>2</sub>NR'R'', -NR'CONR'R'', -CONR'COR'', -NR'C(=N-CN)NR'R'', -C(=N-CN)NR'R'', -NR'C(=N-CN)R'', -NR'C(=C-NO<sub>2</sub>)NR'R'', -SO<sub>2</sub>NR'COR'', -NO<sub>2</sub>, -CO<sub>2</sub>R', -C(C=N-OR')R'', -CR'=CR'R'', -CCR', -S(C=O)(C=N-R')R'', -SF<sub>5</sub>, o -OCF<sub>3</sub>;

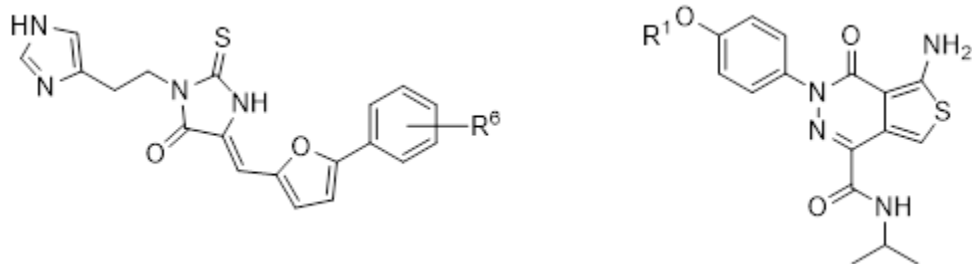
R' y R'' se seleccionan independientemente del grupo que consiste en un enlace, H, N, N-óxido, o -C(=O)R;

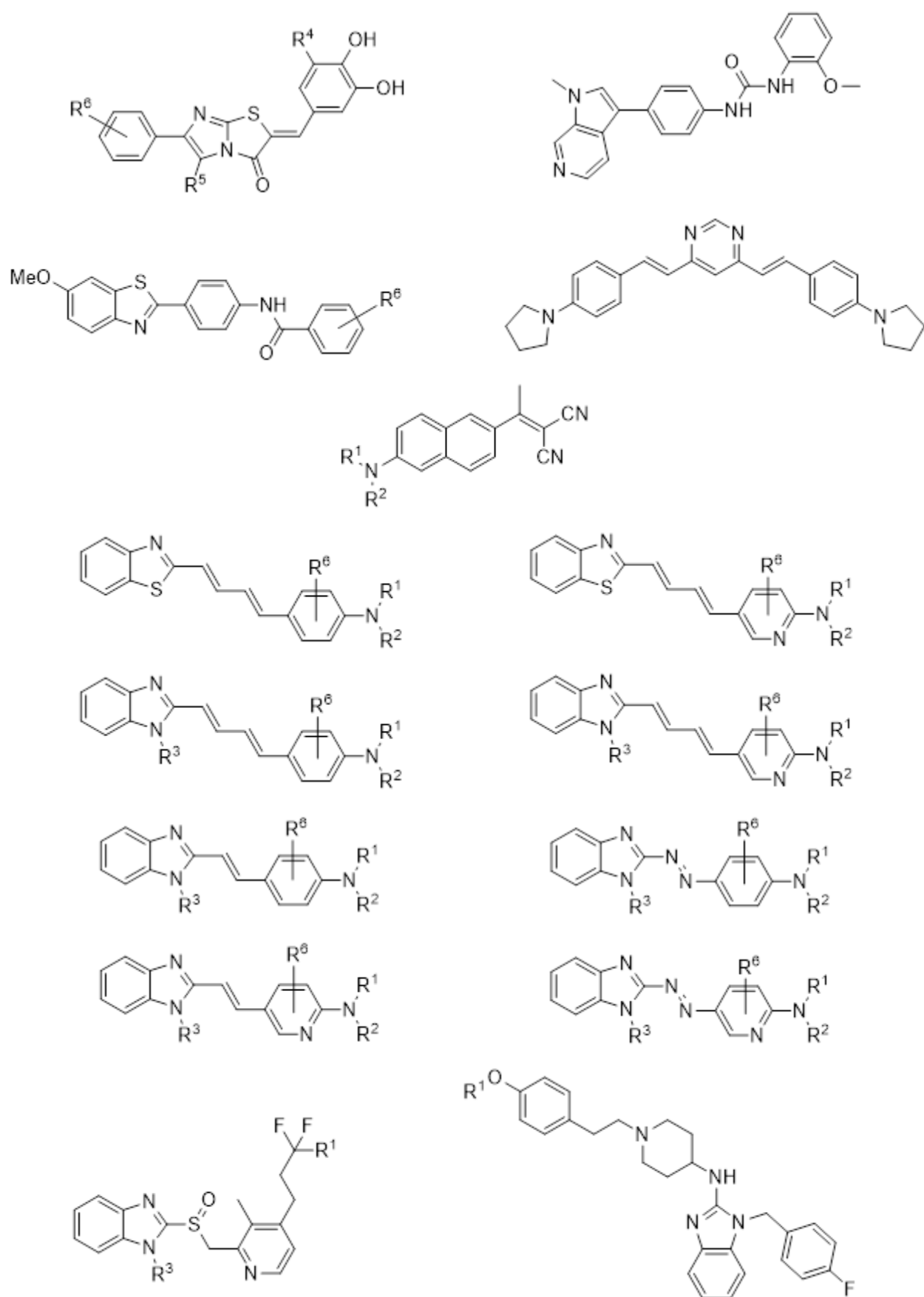
~~~~~ representa un enlace que puede ser estereoespecífico ((R) o (S)) o no estereoespecífico;

y

en donde n es un número entero de 1-4;

la PTM está representada mediante una estructura química seleccionada del grupo que consiste en:





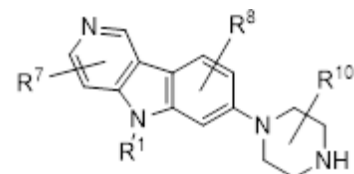
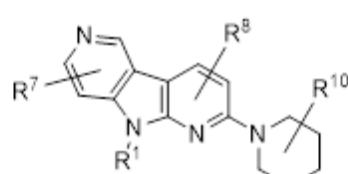
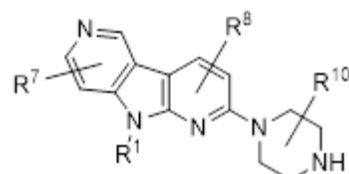
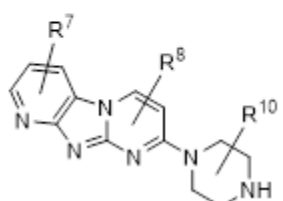
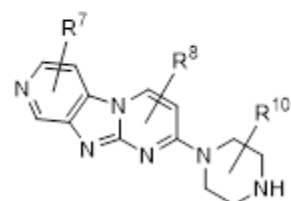
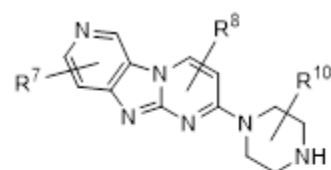
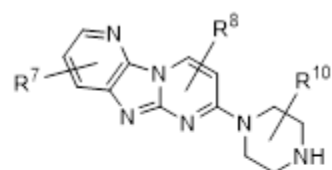
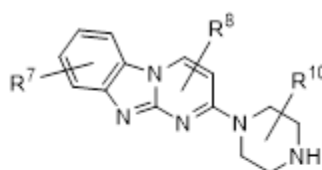
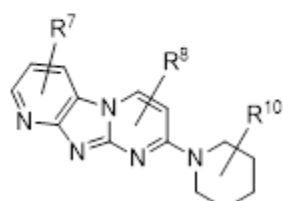
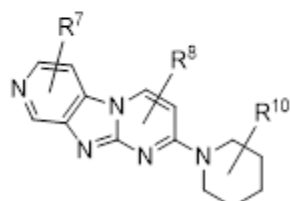
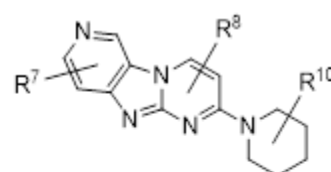
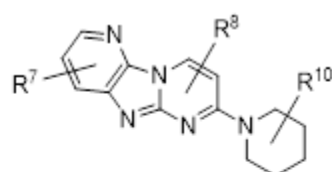
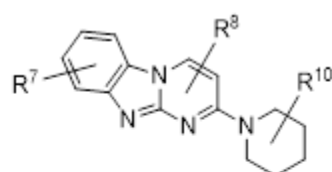
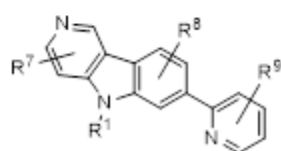
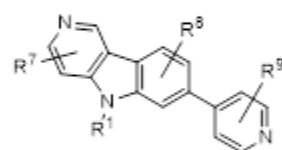
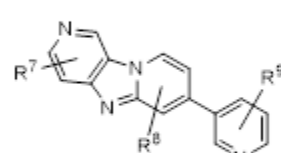
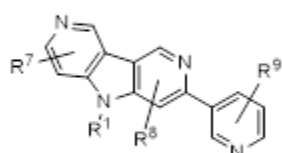
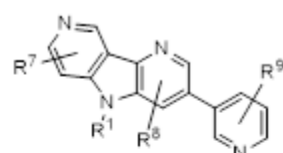
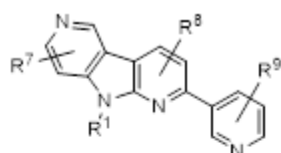
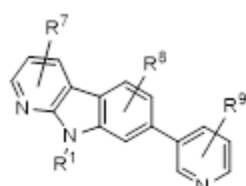
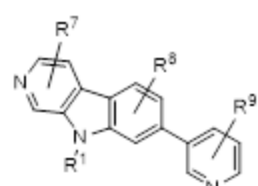
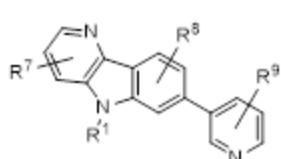
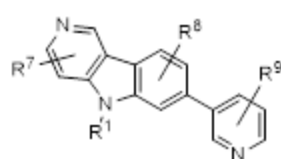
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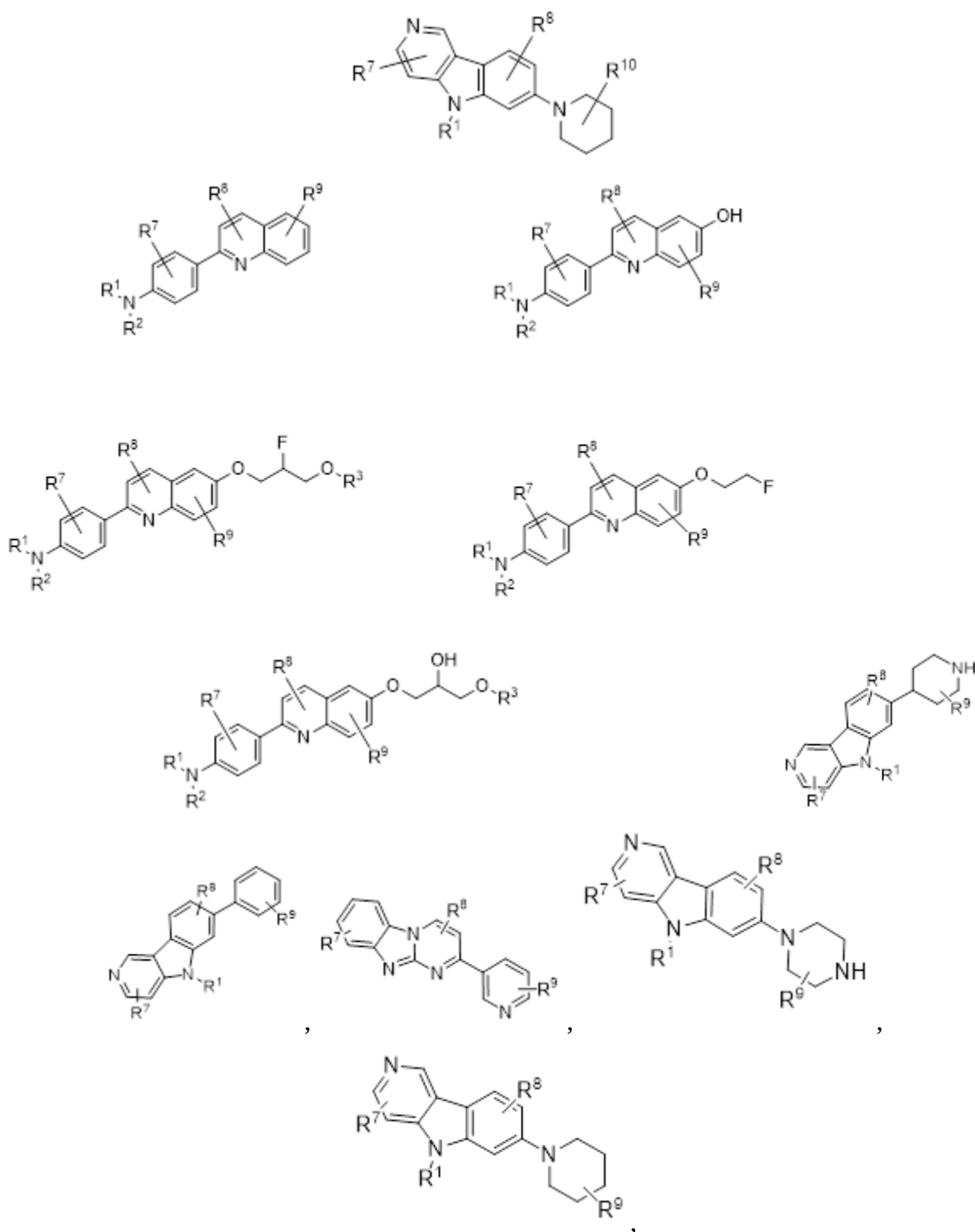
R^1 , R^2 y R^3 se seleccionan independientemente de H, metilo, etilo, 2-fluoroetilo y 2,2,2-trifluoroetilo;

R^4 y R^5 se seleccionan independientemente de H, metilo, etilo y halógeno; y

R^6 es 1 a 2 sustituyentes independientemente seleccionados de H, metilo, etilo y halógeno;

o la PTM se representa mediante una estructura química seleccionada del grupo que consiste en:





en donde:

R¹, R² y R³ se seleccionan independientemente de H, C₁₋₆ alquilo opcionalmente sustituido 1-3 veces con halo; y

R⁷, R⁸, R⁹ y R¹⁰ son 1 a 8 sustituyentes independientemente seleccionados de H, C₁₋₆ alquilo, C₁₋₆ haloalquilo, halógeno, hidroxilo, amino, acetilamino, o ciano; y

el L está representado por la fórmula:



en donde:

A es un grupo que se conecta a la porción ULM o PTM; y

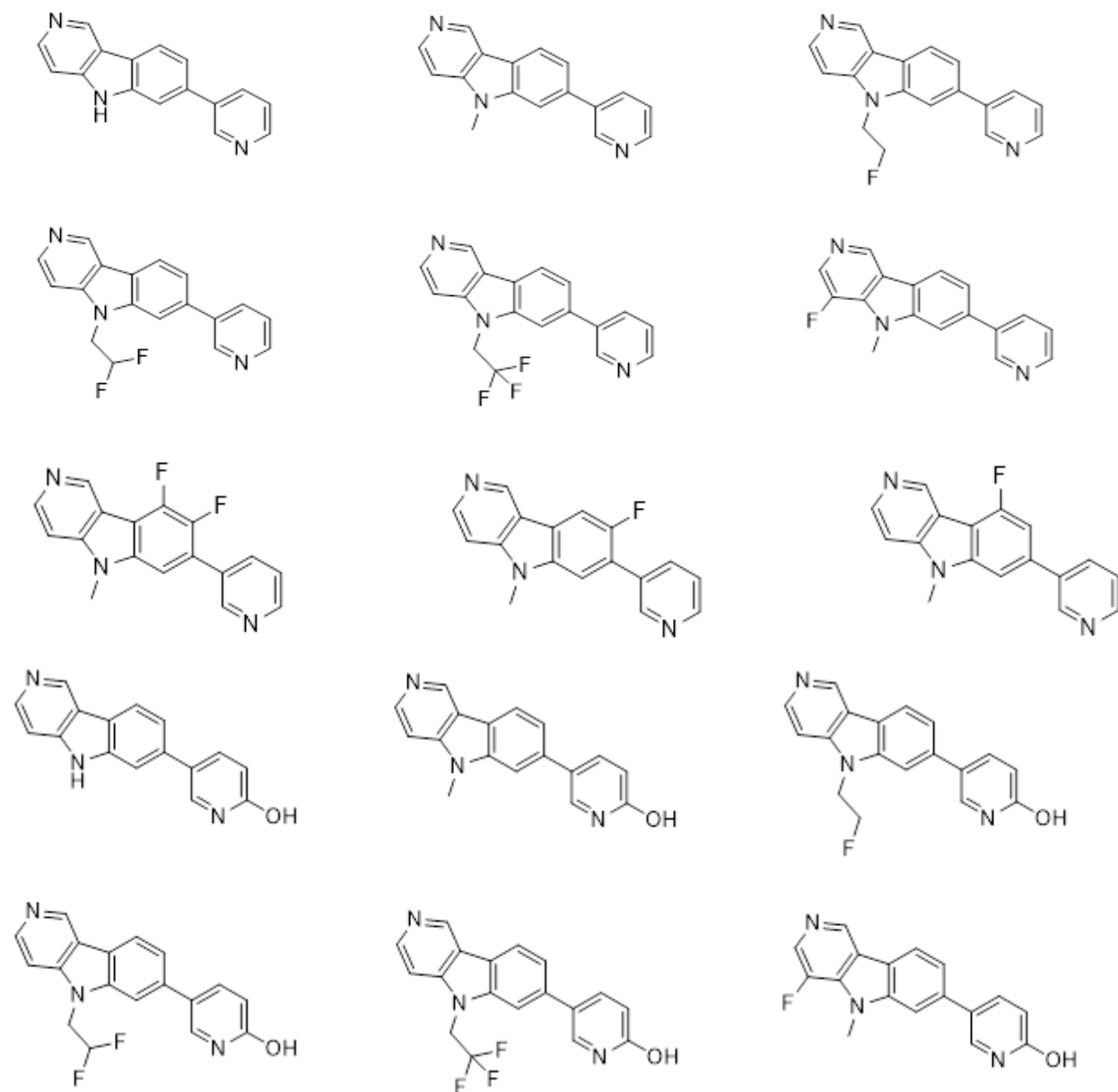
q es un número entero mayor que o igual a 1,

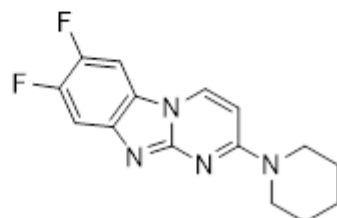
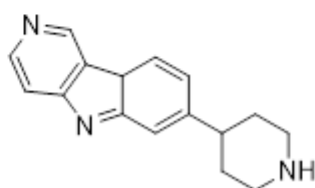
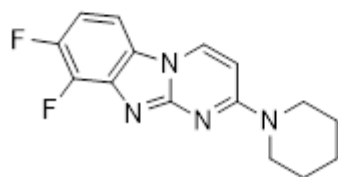
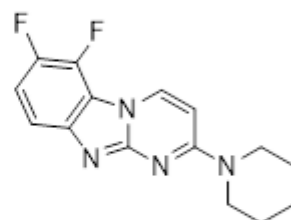
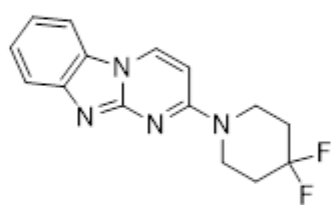
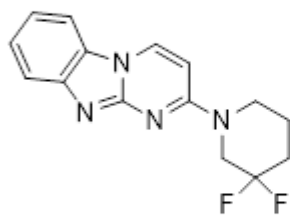
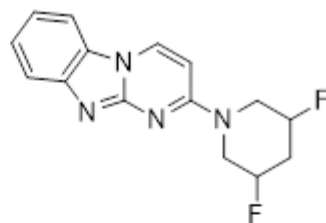
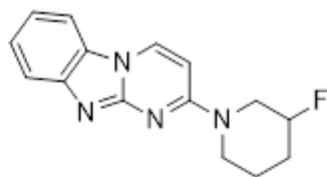
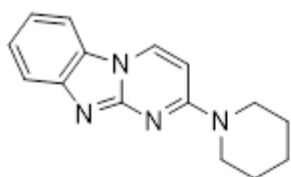
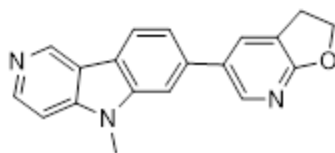
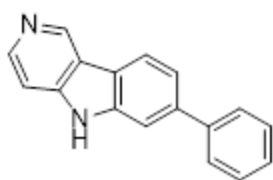
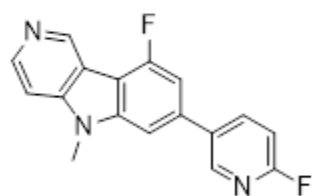
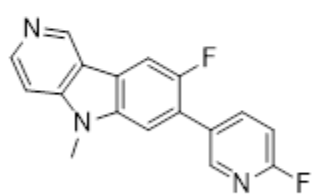
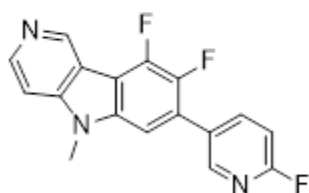
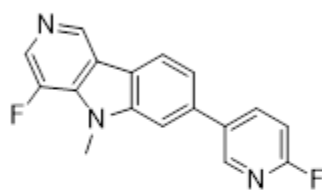
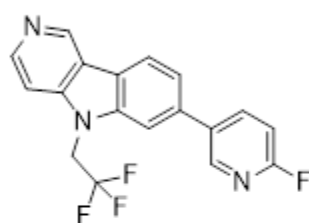
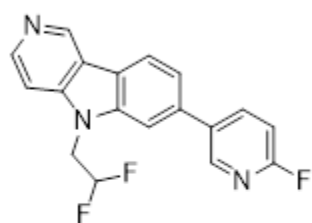
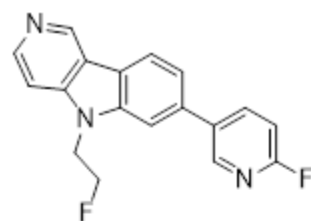
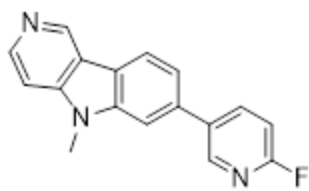
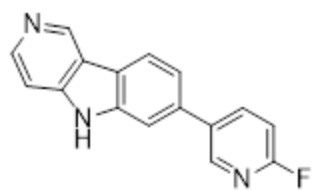
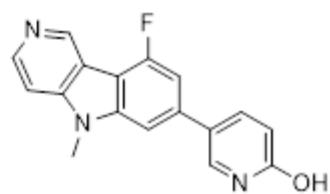
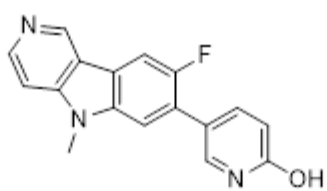
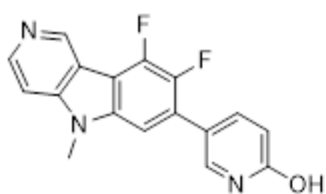
en donde A se selecciona del grupo que consiste en, un enlace, CR^{L1}R^{L2}, O, S, SO, SO₂, NR^{L3}, SO₂NR^{L3}, SONR^{L3}, CONR^{L3}, NR^{L3}CONR^{L4}, NR^{L3}SO₂NR^{L4}, CO, CR^{L1}=CR^{L2}, C≡C, SiR^{L1}R^{L2}, P(O)R^{L1}, P(O)OR^{L1}, NR^{L3}C(=NCN)NR^{L4}, NR^{L3}C(=NCN), NR^{L3}C(=CNO₂)NR^{L4}, cicloalquilo de C₃₋₁₁ opcionalmente sustituido con grupos 0-6 R^{L1} y/o R^{L2}, heterociclilo de 3-11

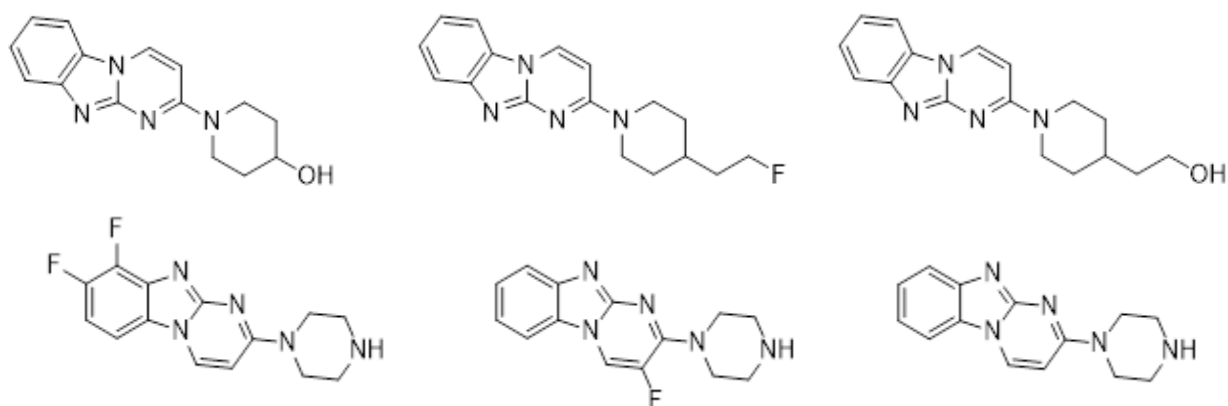
miembros opcionalmente sustituido con grupos 0-6 R^{L1} y/o R^{L2} , C_{6-10} arilo opcionalmente sustituido con grupos 0-6 R^{L1} y/o R^{L2} , heteroarilo de 6-10 miembros opcionalmente sustituido con grupos 0-6 R^{L1} y/o R^{L2} , donde R^{L1} o R^{L2} , cada uno independientemente se unen opcionalmente a otros grupos para formar C_{3-11} cicloalquilo y/o heterocicilo de 3-11 miembros, opcionalmente sustituidos con grupos 0-4 R^{L5} ;

R^{L1} , R^{L2} , R^{L3} , R^{L4} y R^{L5} son, cada uno independientemente, H, halo, alquilo de C_{1-8} , OC_{1-8} alquilo, SC_{1-8} alquilo, NHC_{1-8} alquilo, $N(C_{1-8}$ alquilo) $_2$, C_{3-11} cicloalquilo, heterocicilo de 3-11 miembros, OC_{1-8} cicloalquilo, SC_{1-8} cicloalquilo, NHC_{1-8} cicloalquilo, $N(C_{1-8}$ cicloalquilo) $_2$, $N(C_{1-8}$ cicloalquilo)(C_{1-8} alquilo), OH, NH_2 , SH, SO_2C_{1-8} alquilo, $P(O)(OC_{1-8}$ alquilo)(C_{1-8} alquilo), $P(O)(OC_{1-8}$ alquilo) $_2$, $CC-C_{1-8}$ alquilo, CCH, $CH=CH(C_{1-8}$ alquilo), $C(C_{1-8}$ alquilo)= $CH(C_{1-8}$ alquilo), $C(C_{1-8}$ alquilo)= $C(C_{1-8}$ alquilo) $_2$, $Si(OH)_3$, $Si(C_{1-8}$ alquilo) $_3$, $Si(OH)(C_{1-8}$ alquilo) $_2$, COC_{1-8} alquilo, CO_2H , halógeno, CN, CF_3 , CHF_2 , CH_2F , NO_2 , SF_5 , SO_2NHC_{1-8} alquilo, $SO_2N(C_{1-8}$ alquilo) $_2$, $SONHC_{1-8}$ alquilo, $SON(C_{1-8}$ alquilo) $_2$, $CONHC_{1-8}$ alquilo, $CON(C_{1-8}$ alquilo) $_2$, $N(C_{1-8}$ alquilo)CONH(C_{1-8} alquilo), $N(C_{1-8}$ alquilo)CON(C_{1-8} alquilo) $_2$, $NHCONH(C_{1-8}$ alquilo), $NHCON(C_{1-8}$ alquilo) $_2$, $NHCONH_2$, $N(C_{1-8}$ alquilo) $SO_2NH(C_{1-8}$ alquilo), $N(C_{1-8}$ alquilo) $SO_2N(C_{1-8}$ alquilo) $_2$, $NH SO_2NH(C_{1-8}$ alquilo), $NH SO_2N(C_{1-8}$ alquilo) $_2$, $NH SO_2NH_2$.

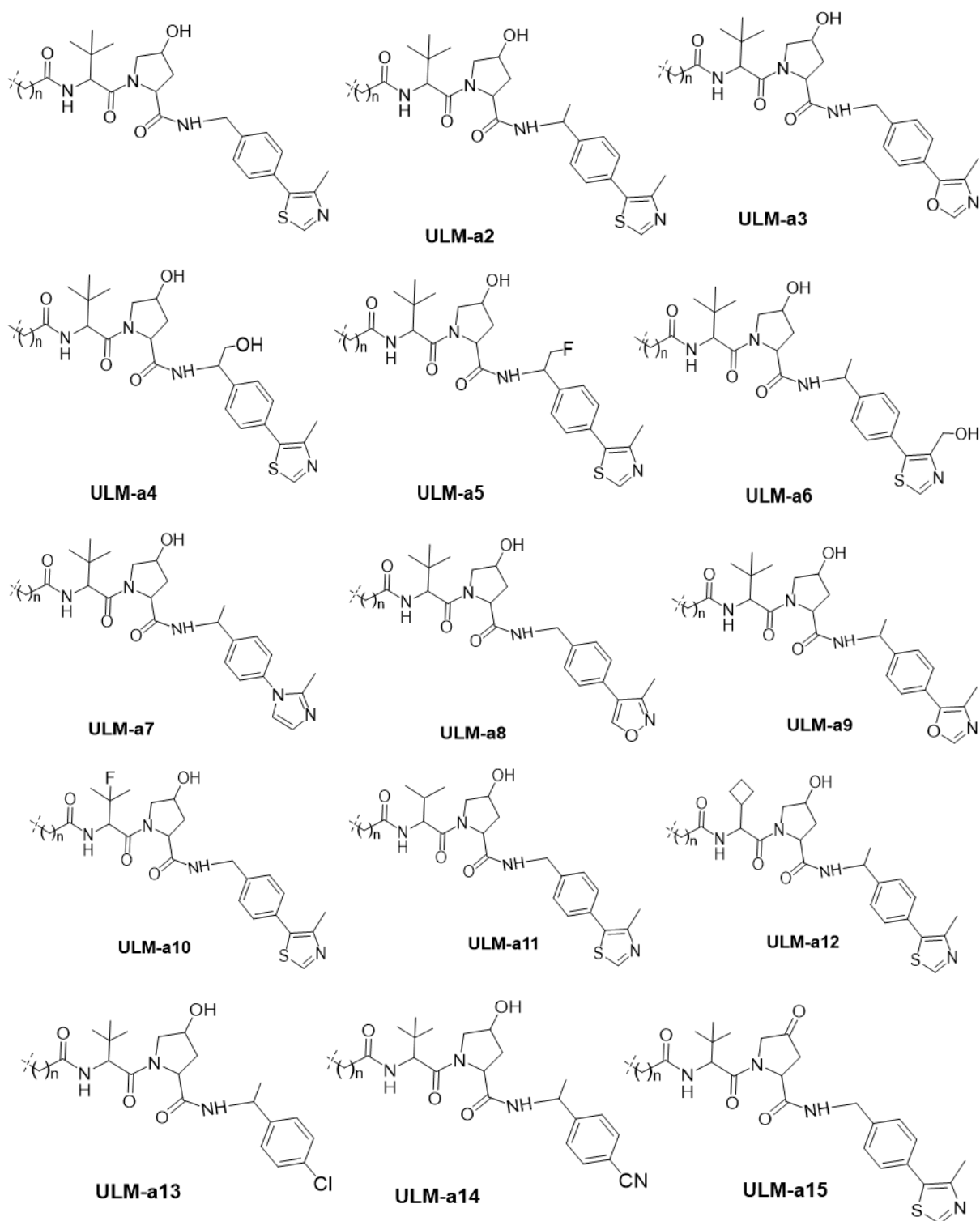
2. El compuesto de conformidad con la reivindicación 1, en donde la PTM se representa mediante una estructura química seleccionada del grupo que consiste en:

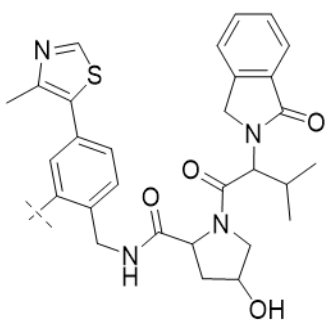




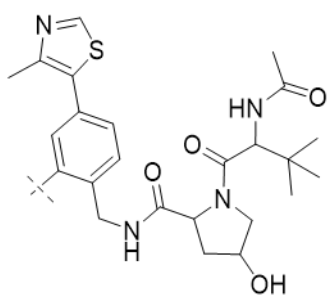


3. El compuesto de conformidad con la reivindicación 1 o reivindicación 2, en donde la ULM comprende un grupo seleccionado de la estructura que consiste en:

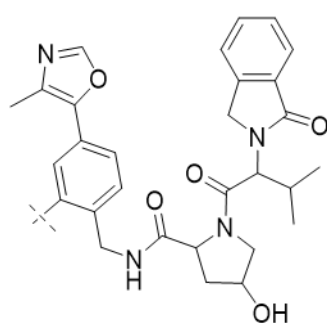




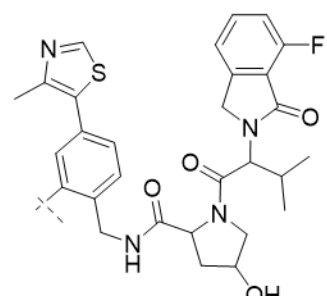
UTM-b1



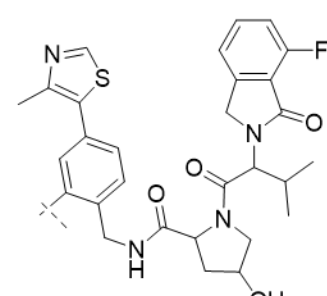
UTM-b2



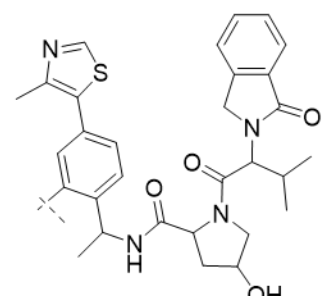
UTM-b3



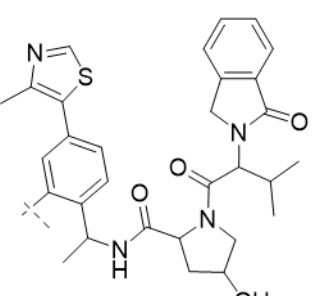
UTM-b4



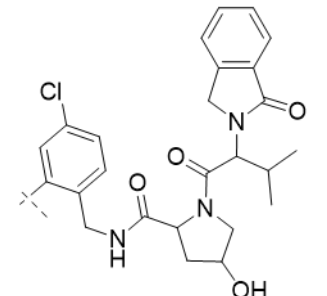
UTM-b5



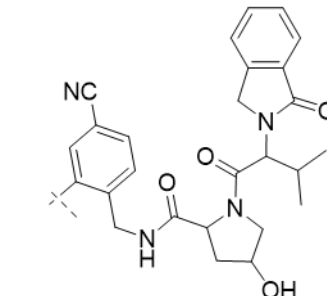
UTM-b6



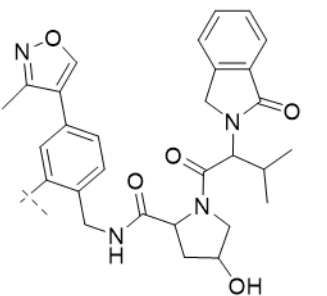
UTM-b7



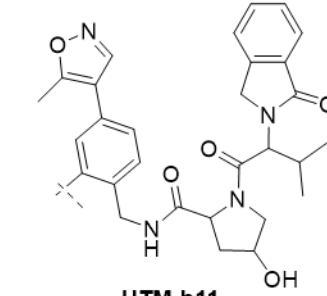
UTM-b8



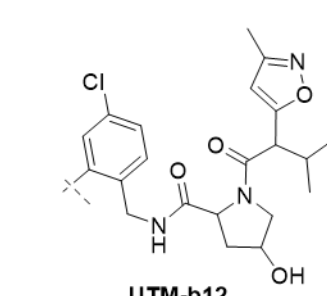
UTM-b9



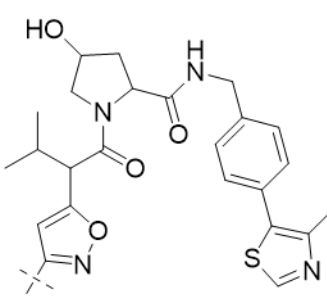
UTM-b10



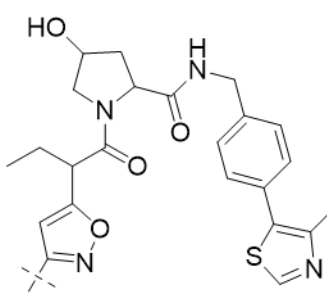
UTM-b11



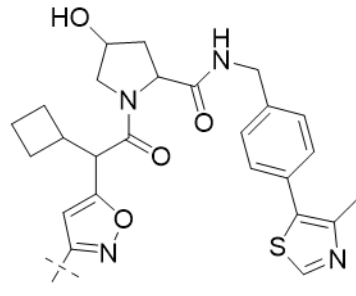
UTM-b12



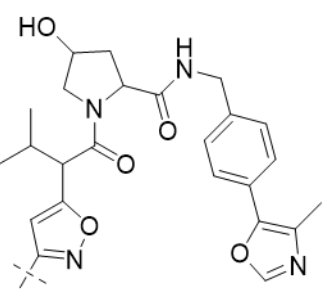
UTM-c1



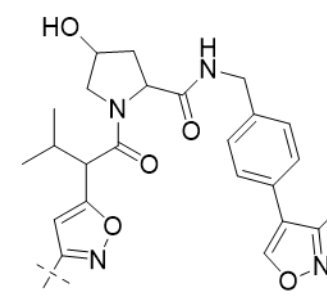
UTM-c2



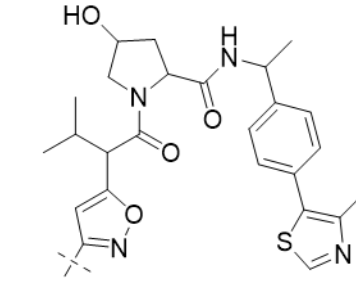
UTM-c3



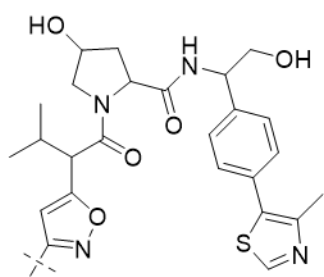
UTM-c4



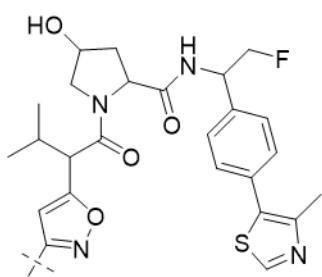
UTM-c5



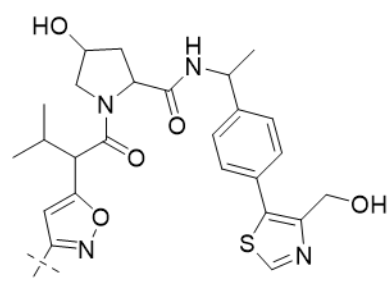
UTM-c6



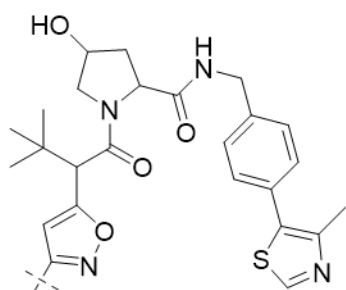
UTM-c7



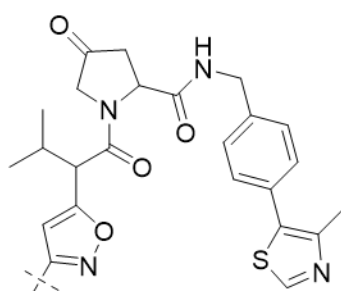
UTM-c8



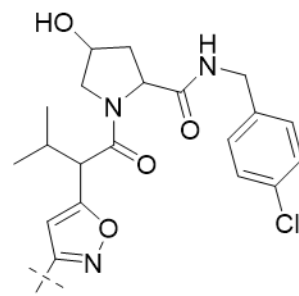
UTM-c9



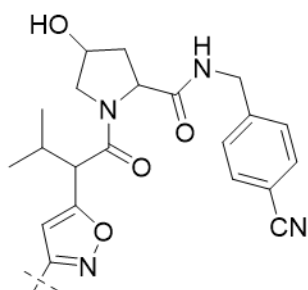
UTM-c10



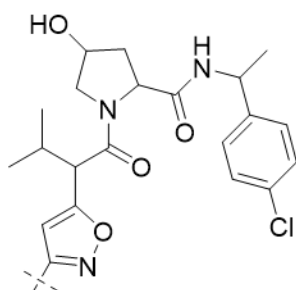
UTM-c11



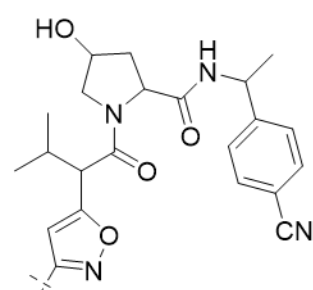
UTM-c12



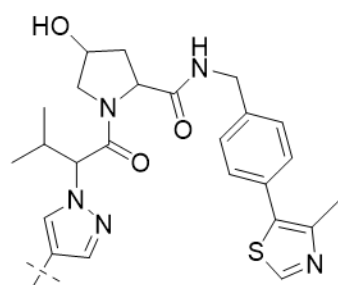
UTM-c13



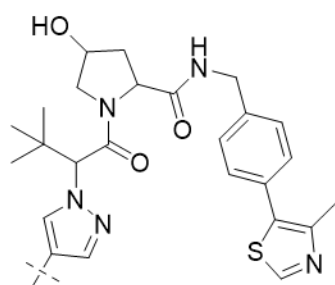
UTM-c14



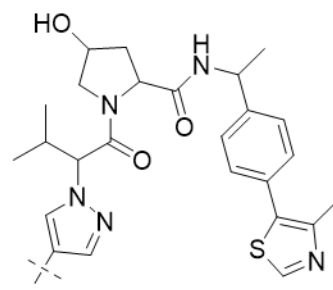
UTM-c15



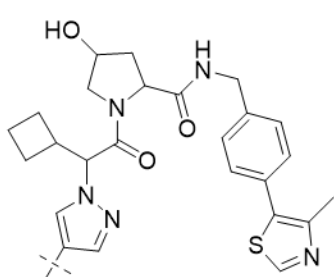
UTM-d1



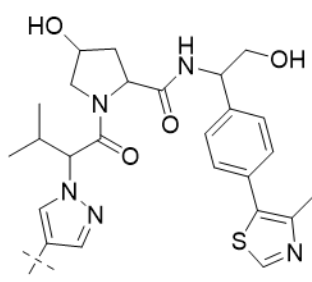
UTM-d2



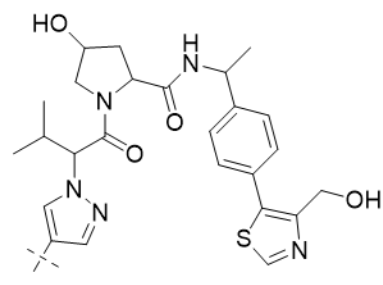
UTM-d3



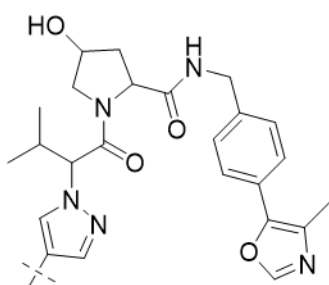
UTM-d4



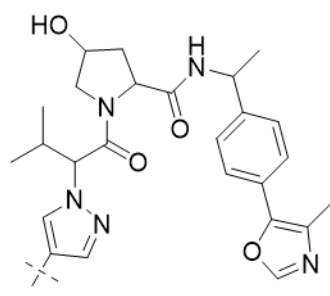
UTM-d5



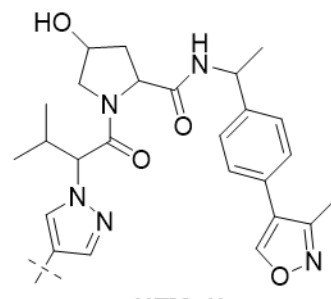
UTM-d6



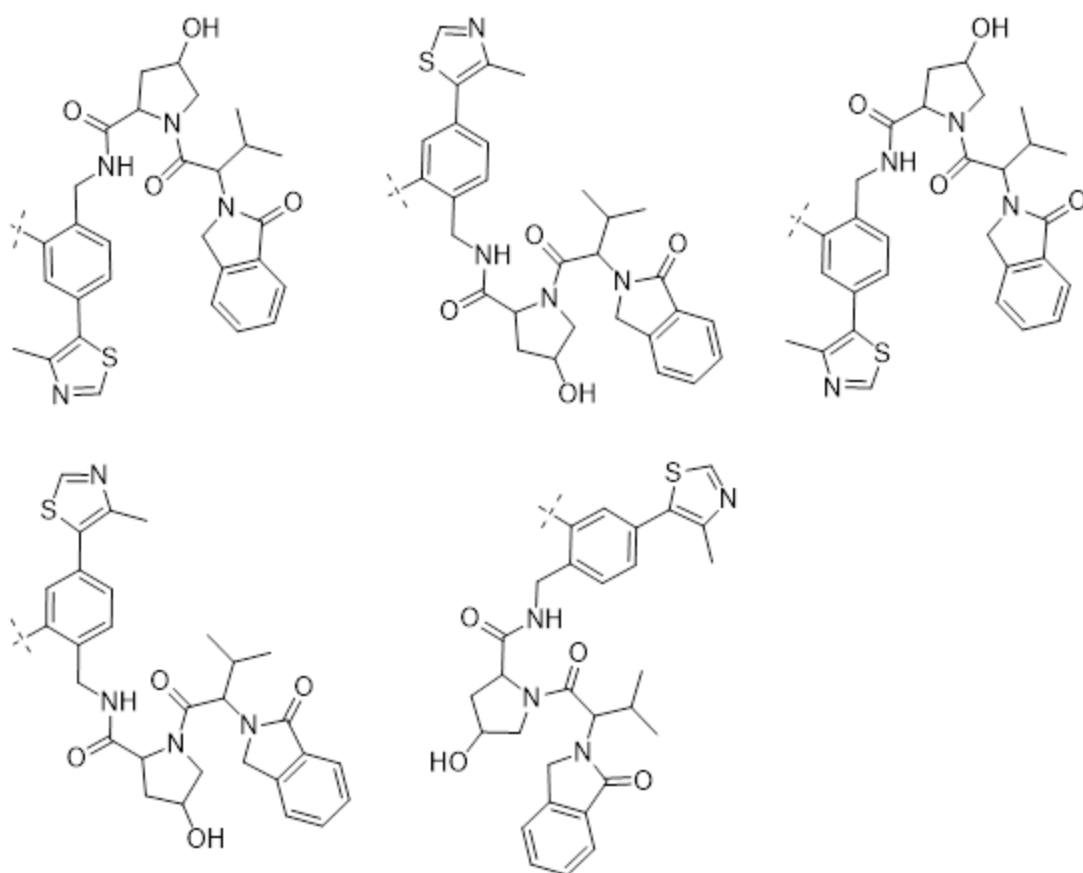
UTM-d7



UTM-d8

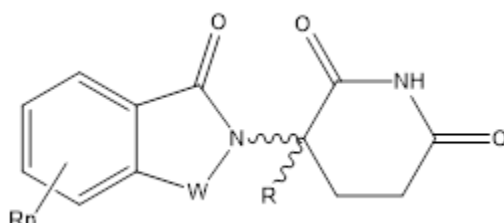


UTM-d9



en donde el anillo fenilo en la ULM-a1 hasta la ULM -a15, ULM -b1 hasta la ULM-b12, ULM-c1 hasta la ULM-c15 y ULM-d1 hasta la ULM-d9 se sustituye opcionalmente con fluor, y en donde la línea discontinua indica el punto de acoplamiento de la porción de enlazador químico.

4. El compuesto de conformidad con la reivindicación 1 o reivindicación 2, en donde la CLM tiene una estructura química representada por:



en donde:

W se selecciona independientemente del grupo CH₂, C=O, y NH;

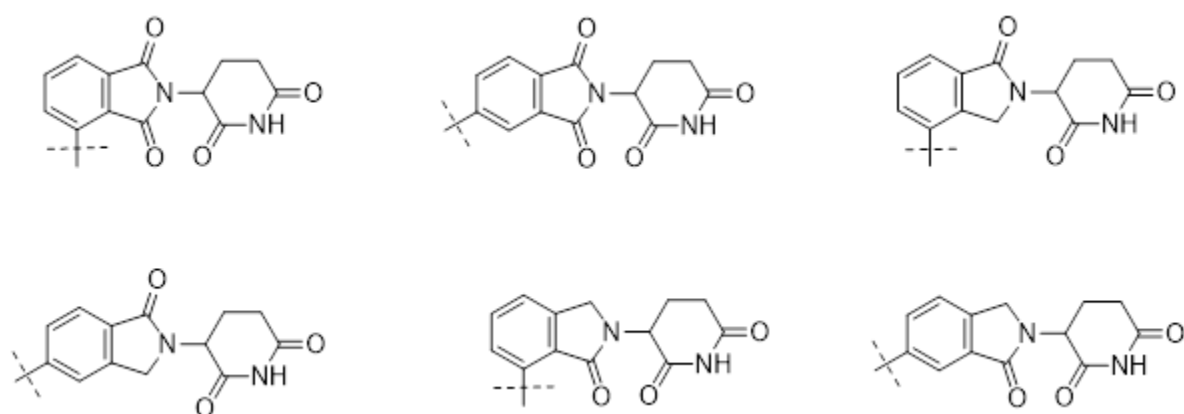
R se selecciona independientemente de un H, metilo, alquilo;

~~~~~ representa un enlace que puede ser estereoespecífico ((R) o (S)) o no estereoespecífico;

y

Rn comprende un grupo enlazador químico (L).

5. El compuesto de conformidad con cualquiera de las reivindicaciones 1, 2, o 4, en donde la CLM tiene una estructura química representada por:



en donde las líneas discontinuas indican los puntos de acoplamiento del enlazador.

6. El compuesto de conformidad con cualquiera de las reivindicaciones 1 a 5, en donde el enlazador (L) comprende un grupo representado por una estructura general seleccionada del grupo que consiste en:

-N(R)-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-OCH<sub>2</sub>-,

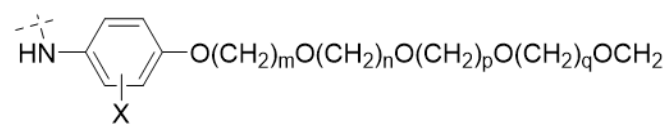
-O-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-OCH<sub>2</sub>-,

-O-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-O-;

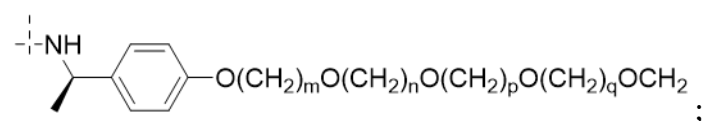
-N(R)-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-O-;

-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-O-;

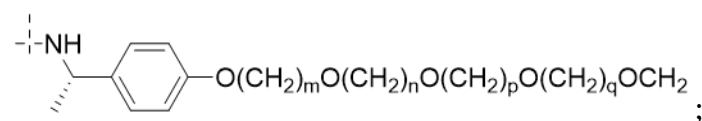
-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-OCH<sub>2</sub>-;



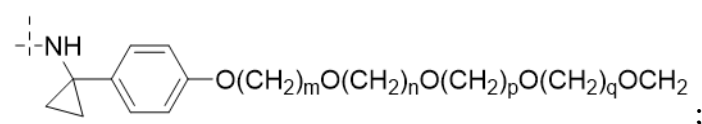
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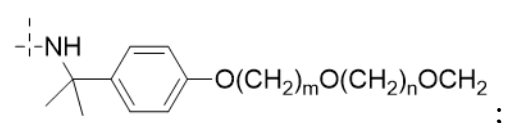
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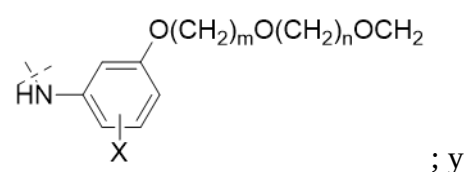
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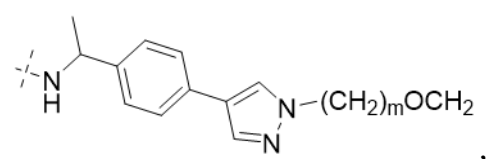
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;

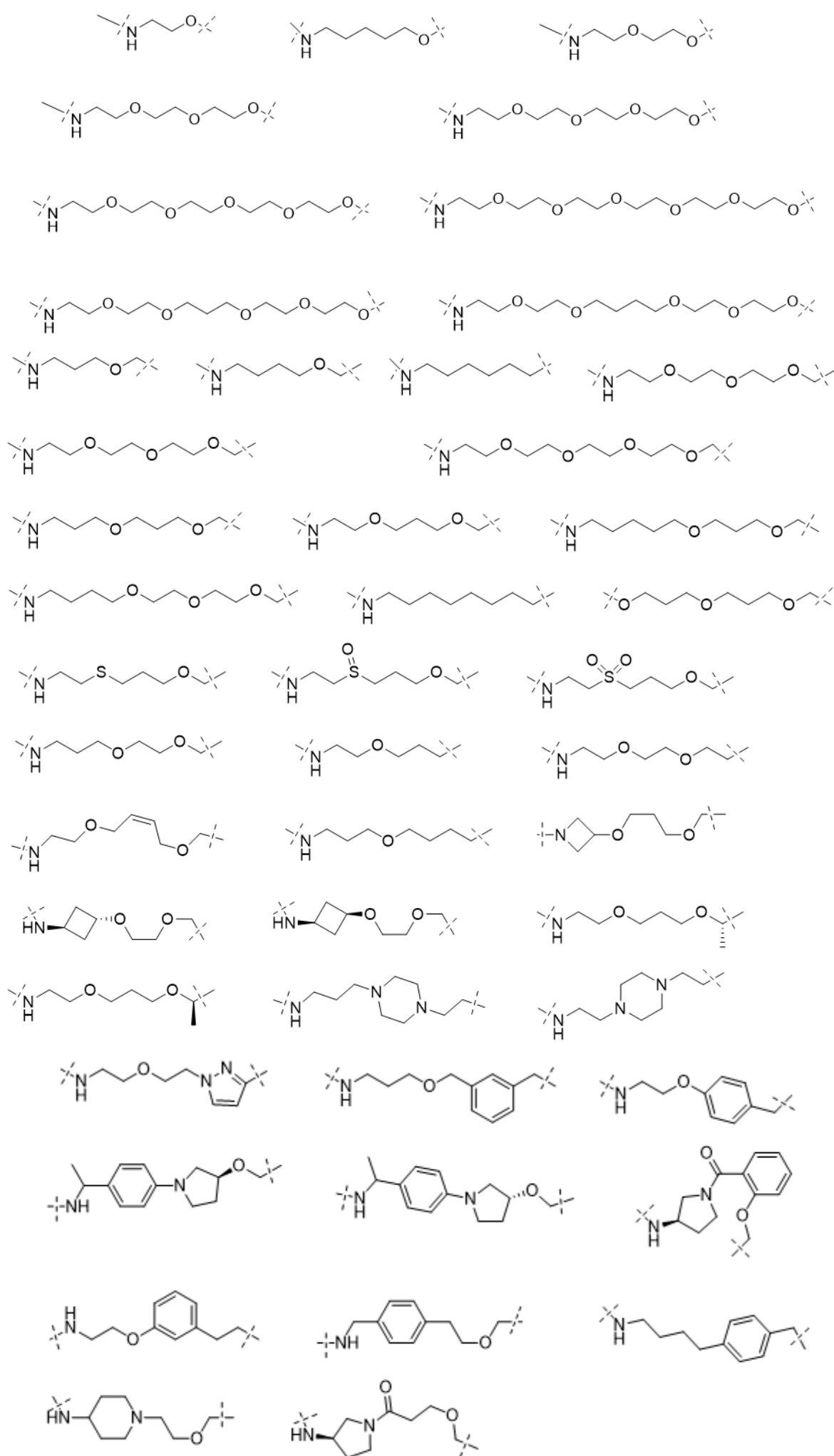


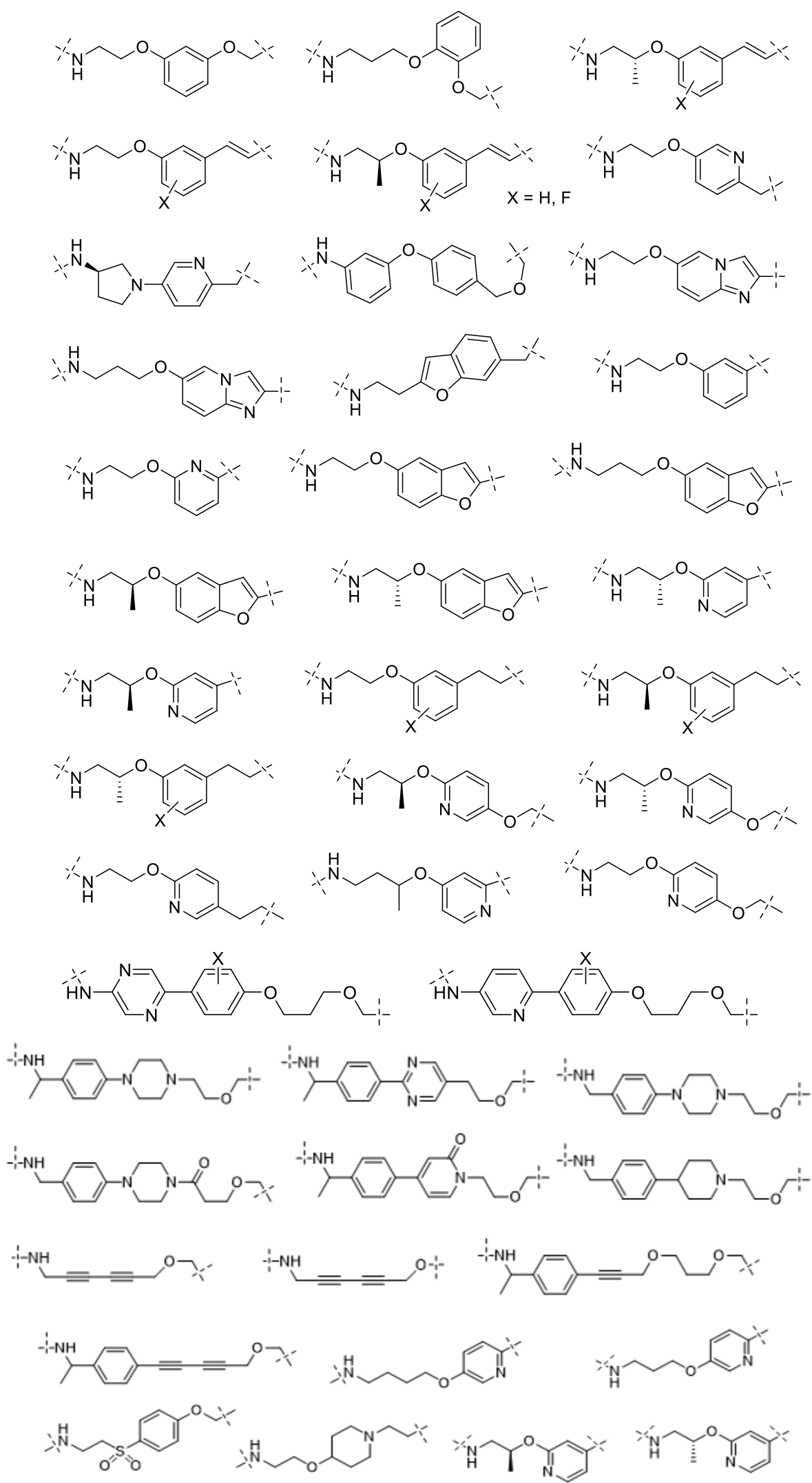
; y

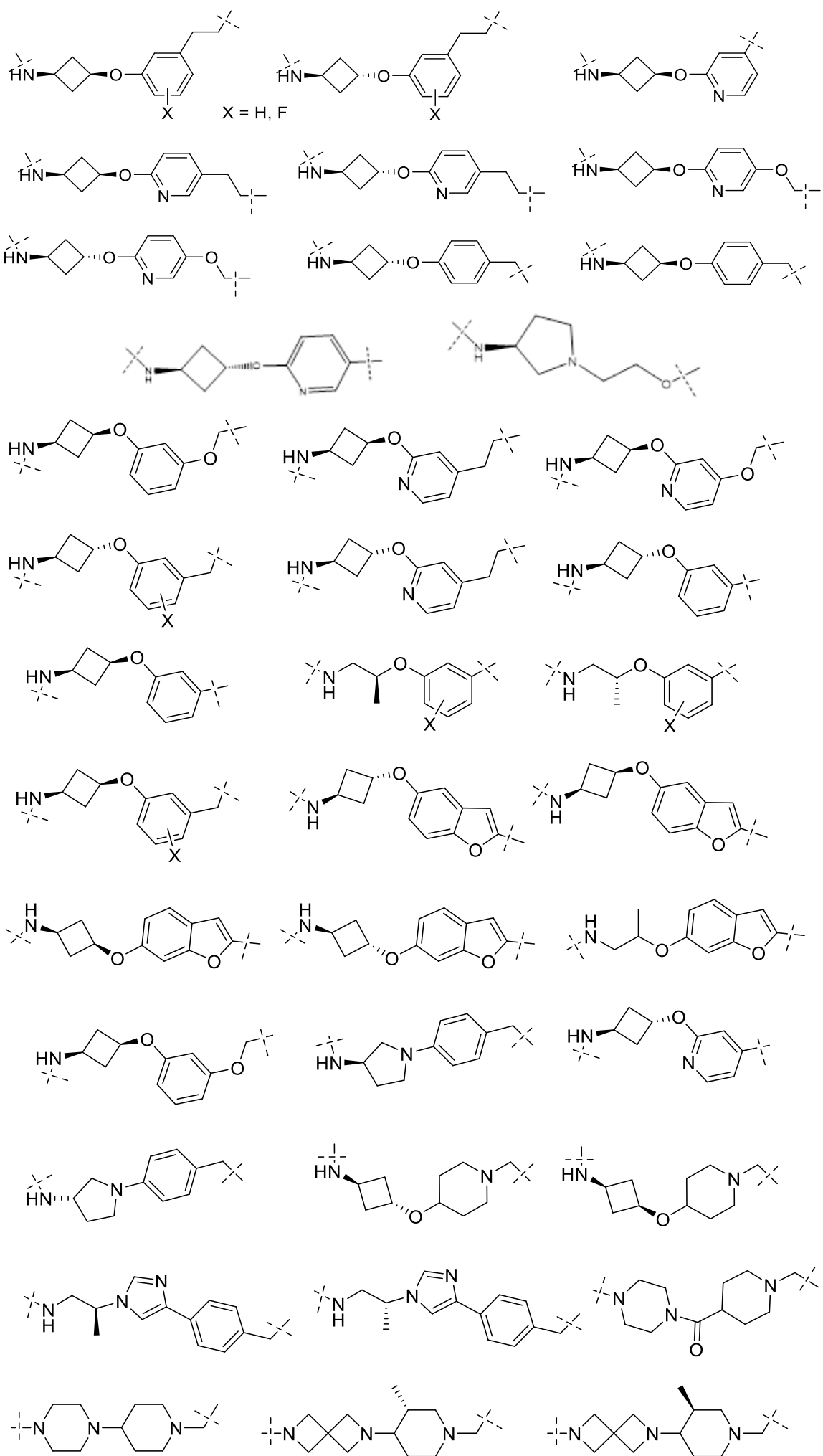


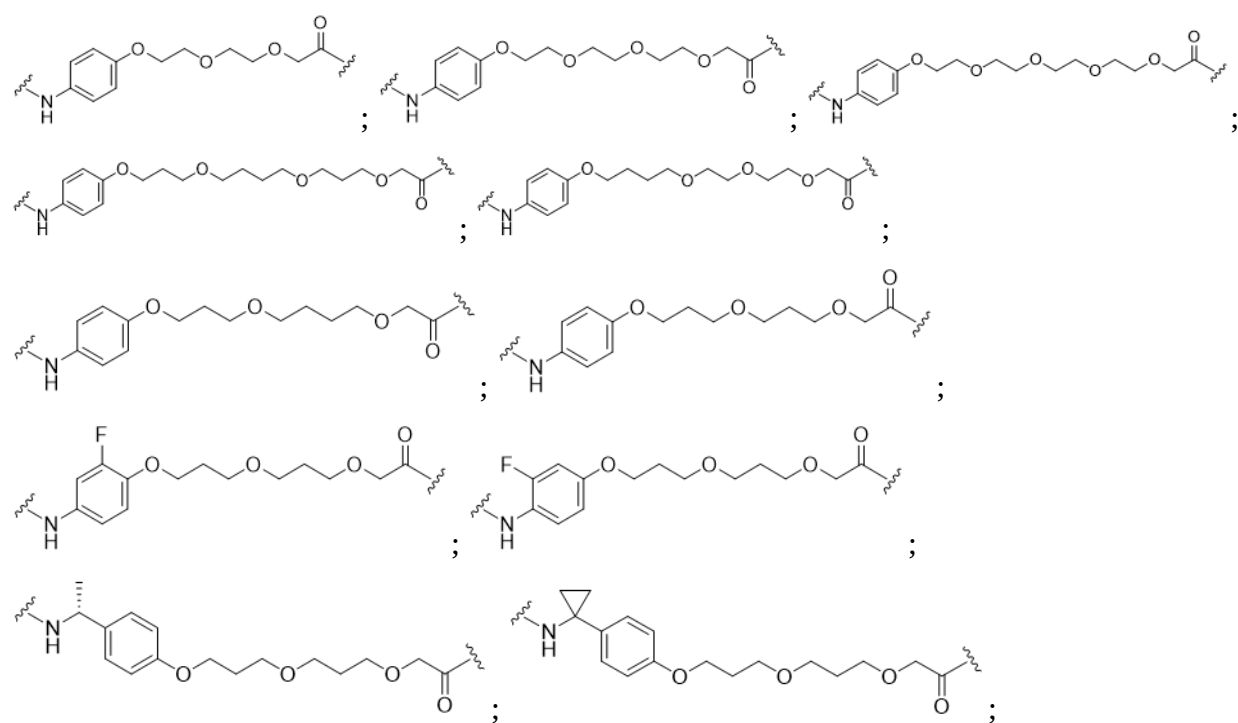
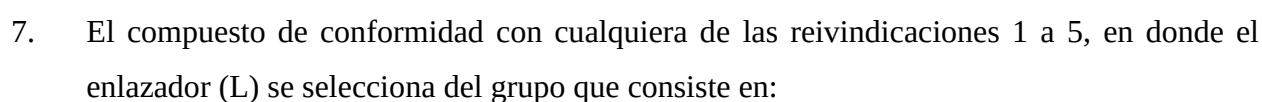
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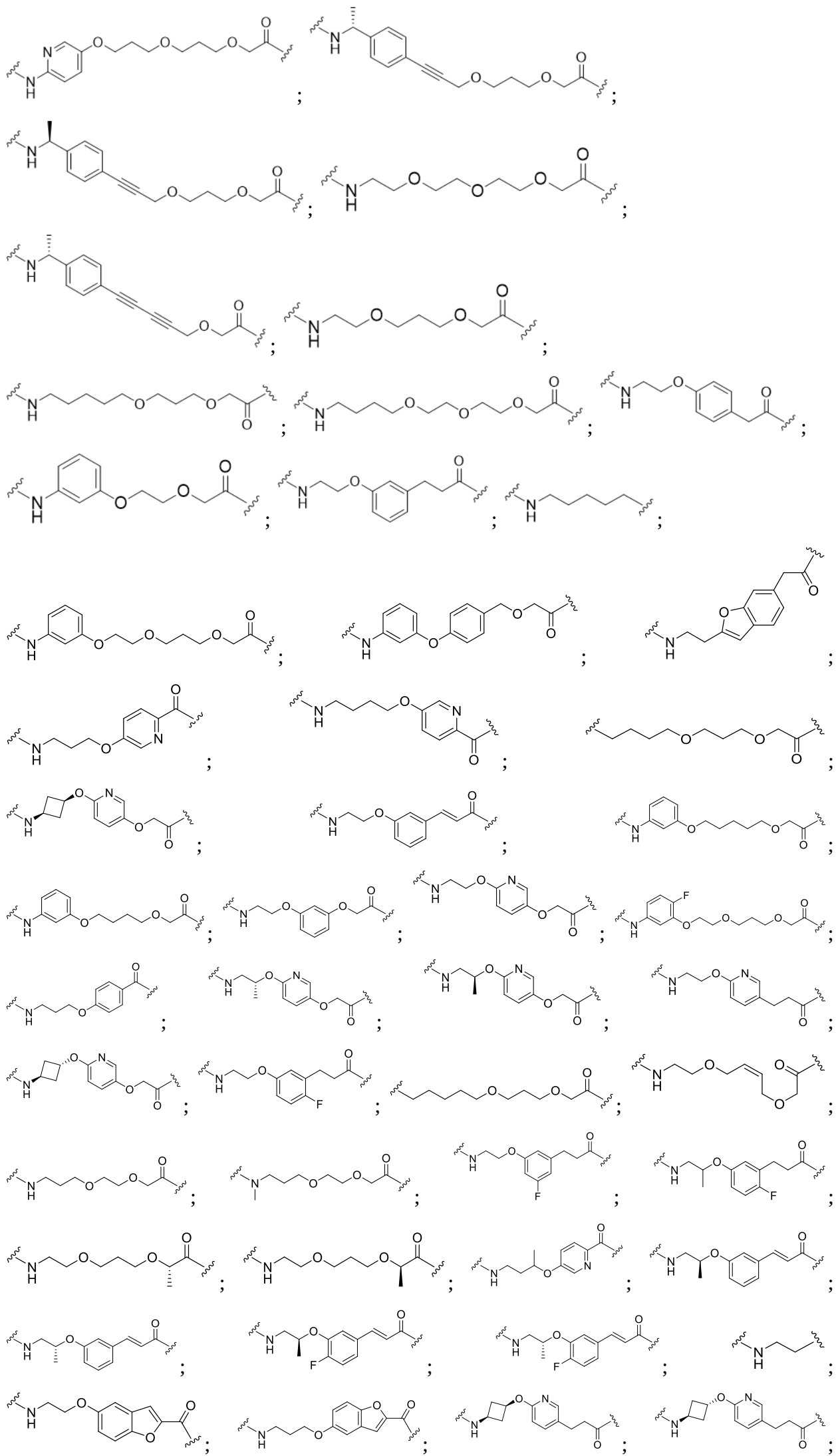
en donde cada m, n, o, p, q, y r, es independientemente 0, 1, 2, 3, 4, 5, 6, con la salvedad de que cuando el número es cero, no hay enlace N-O o O-O; R se selecciona del grupo H, metilo o etilo, y X se selecciona del grupo H o F;

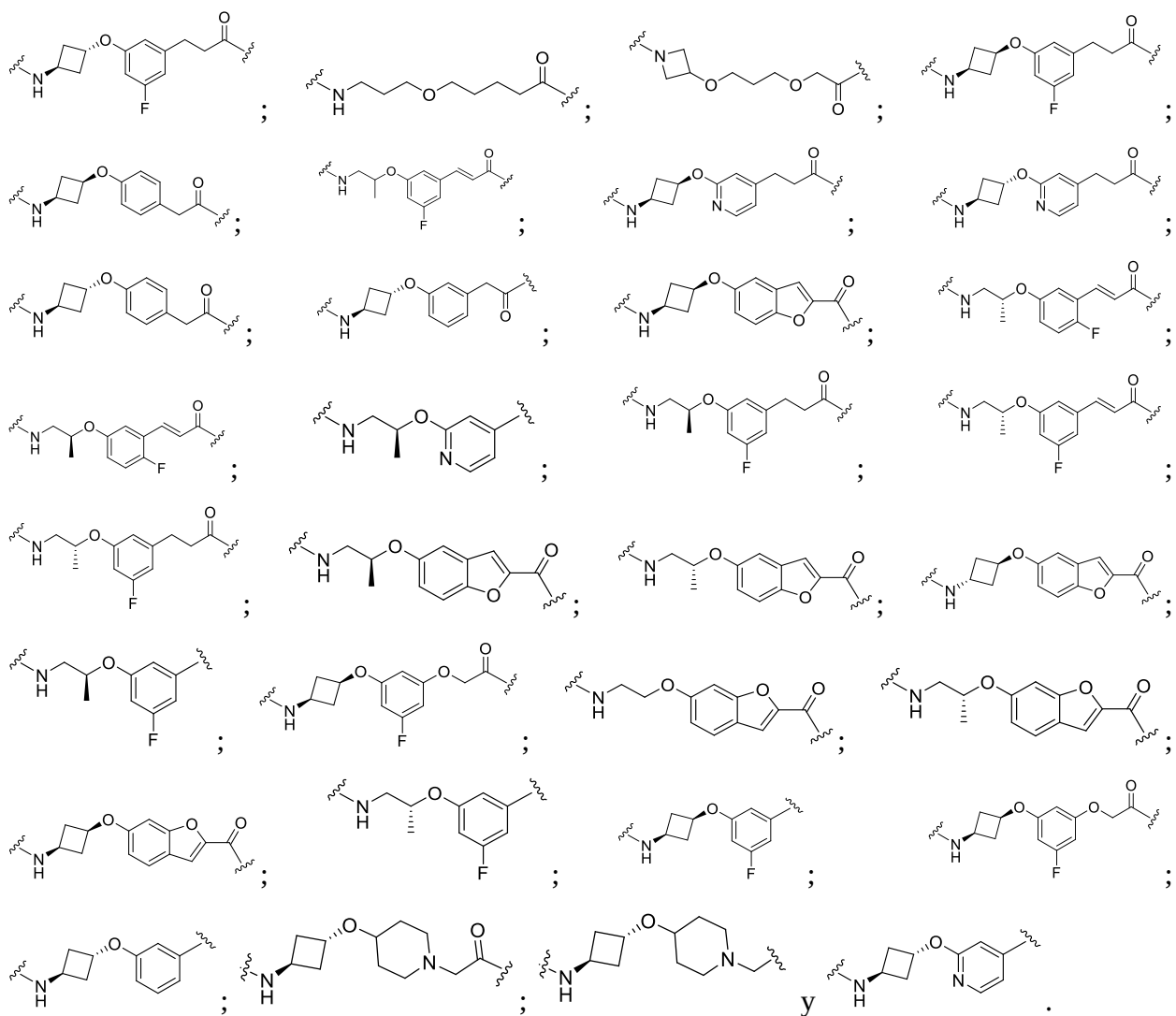




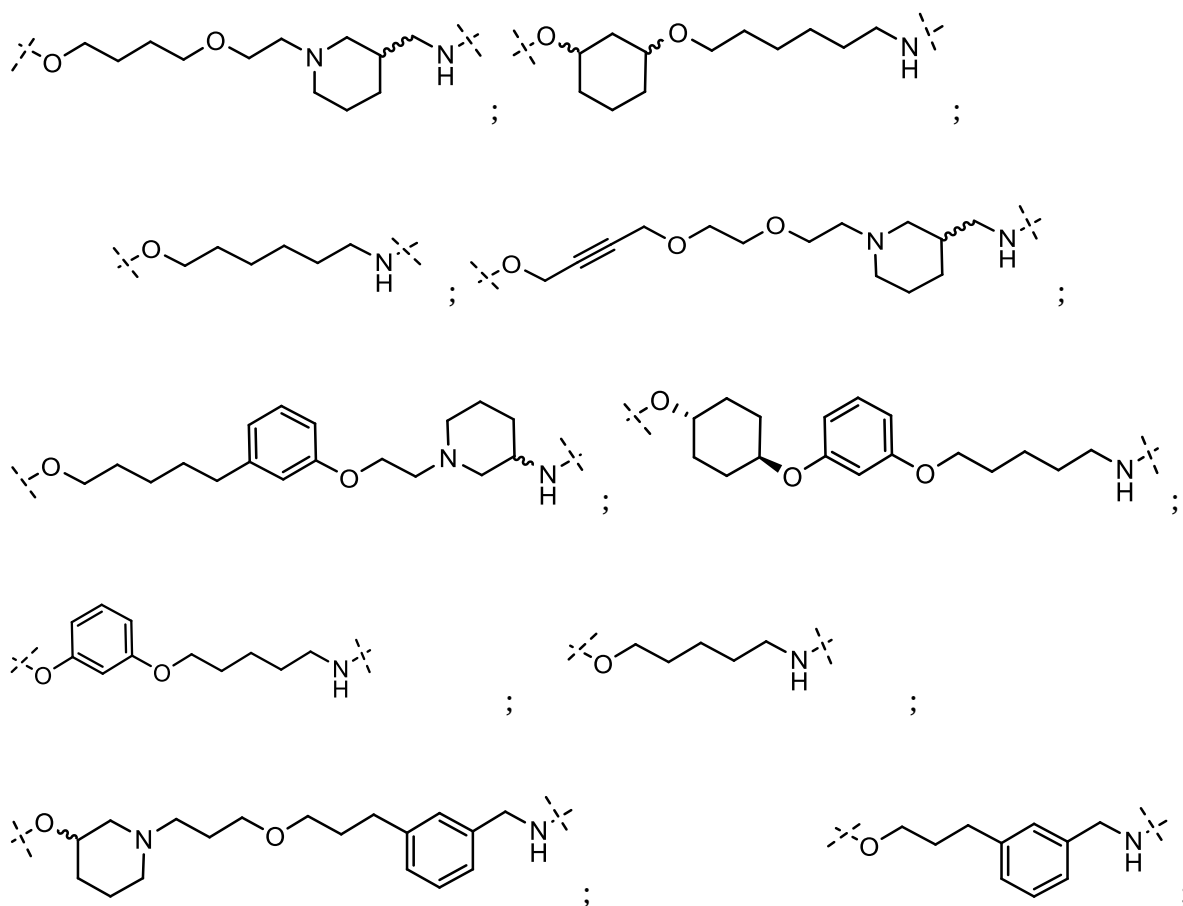


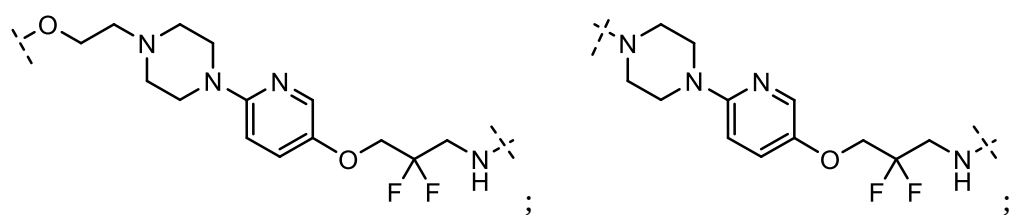
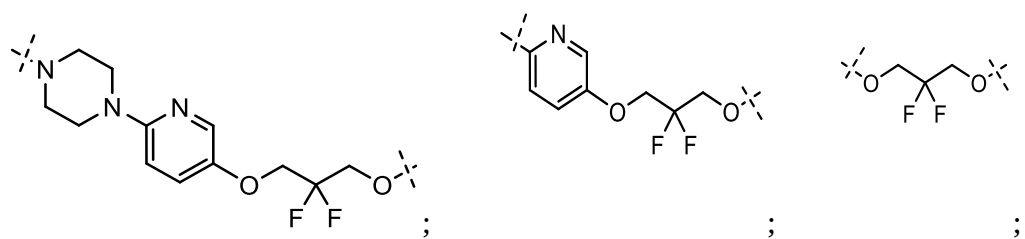
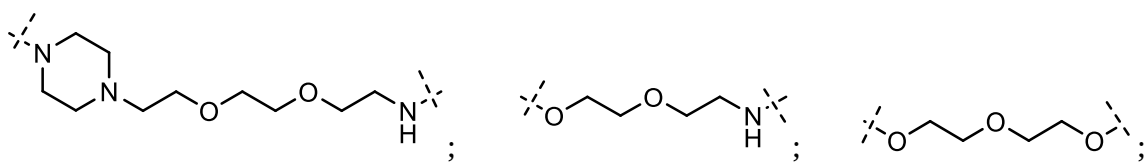
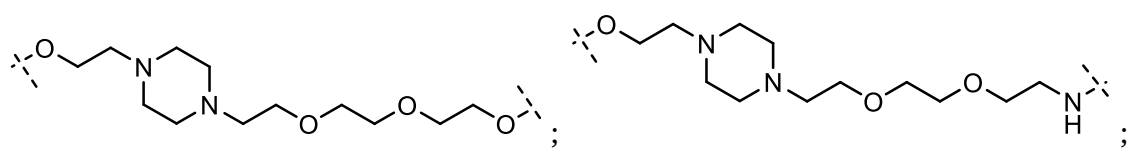
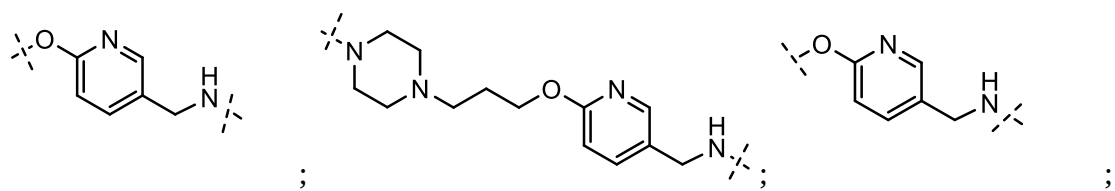
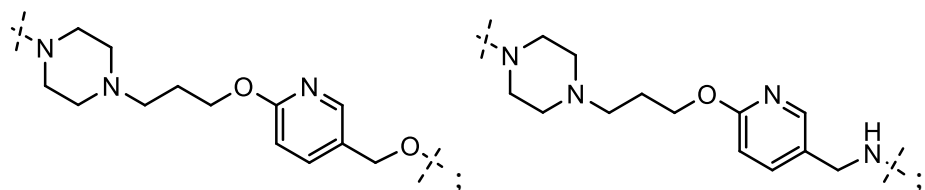
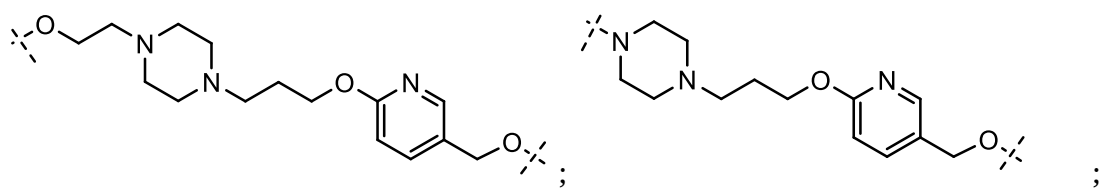
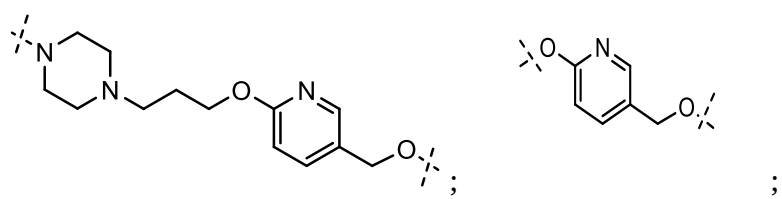


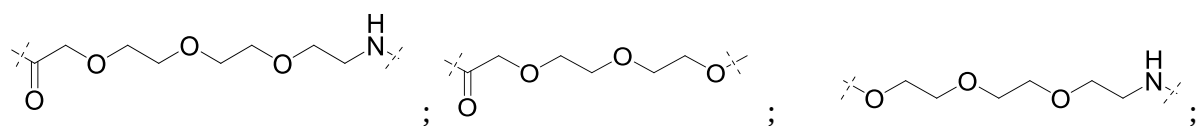
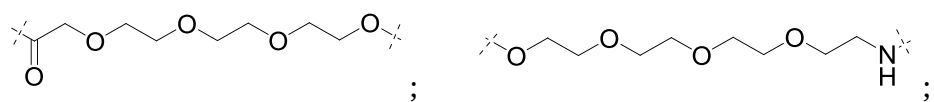
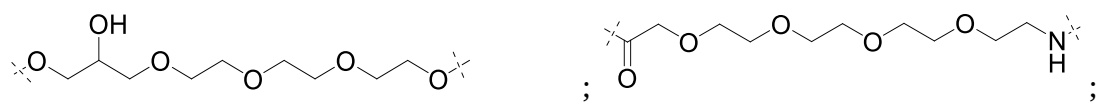
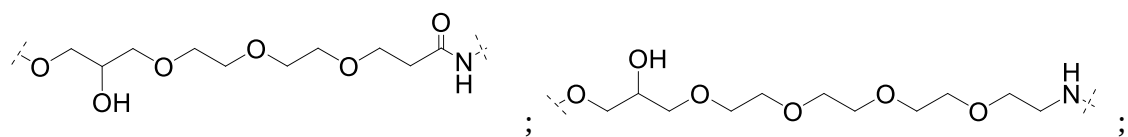
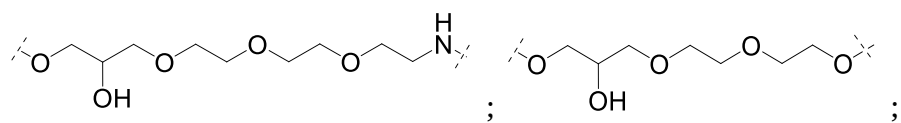
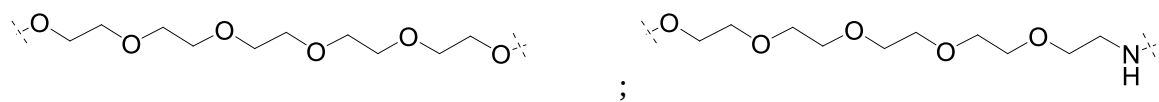
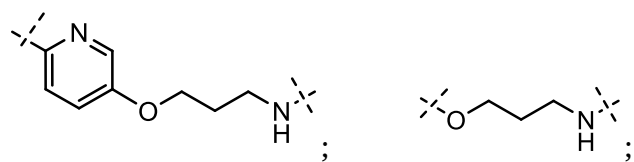
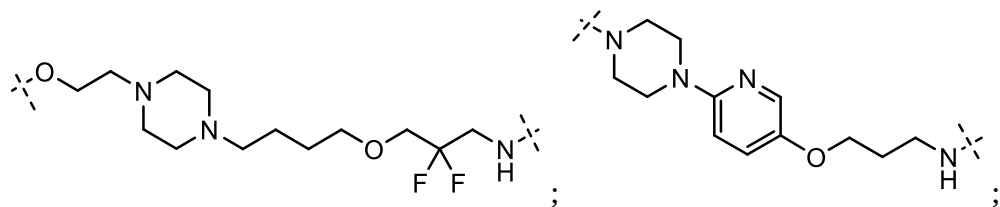
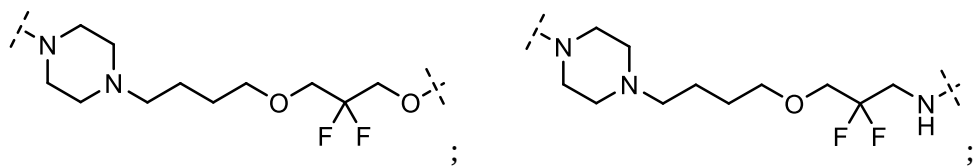
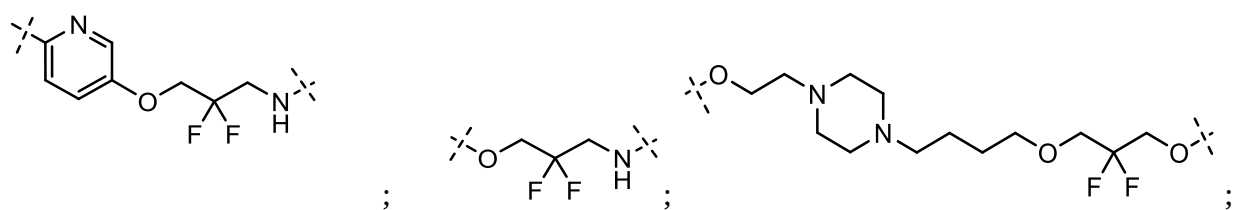


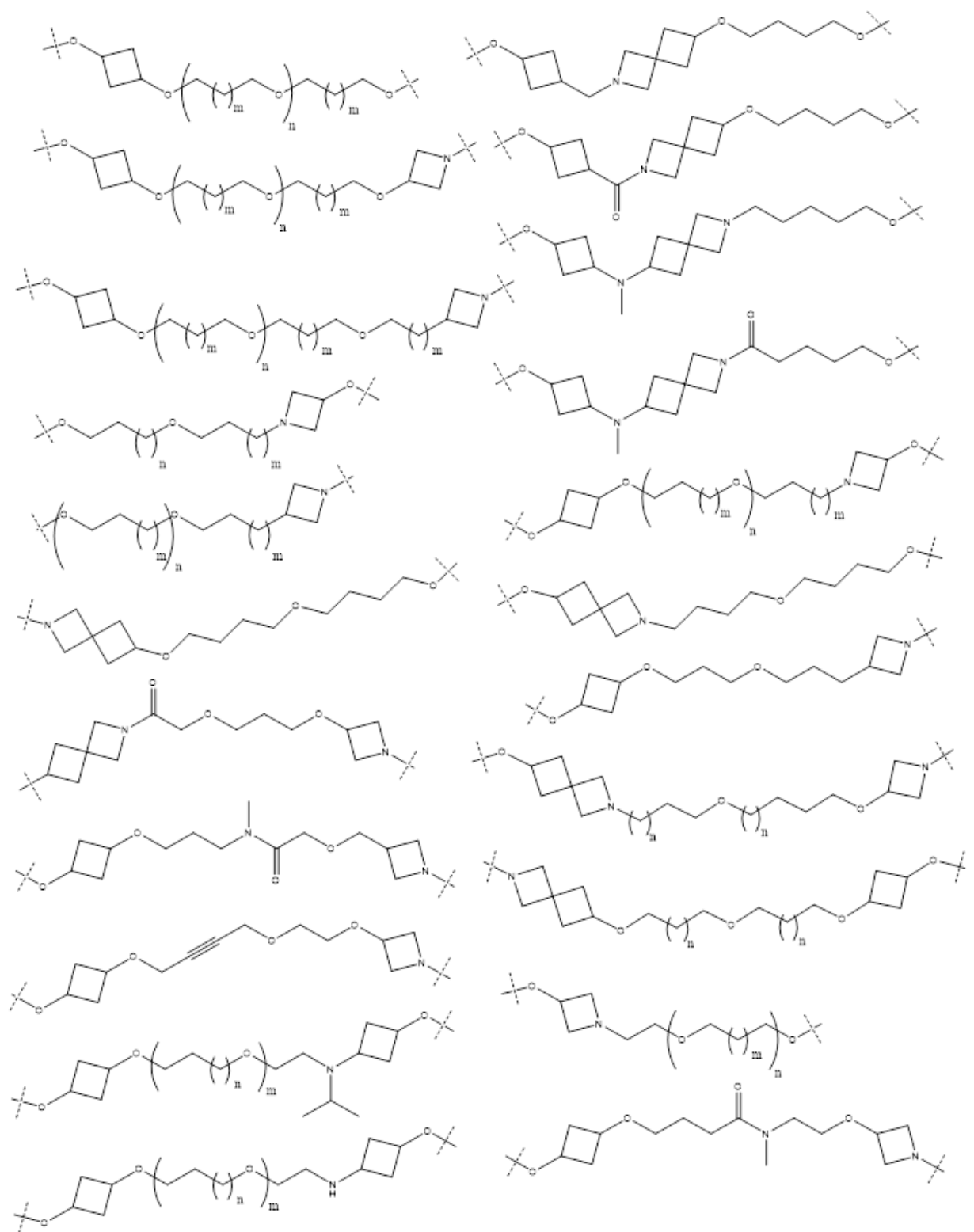


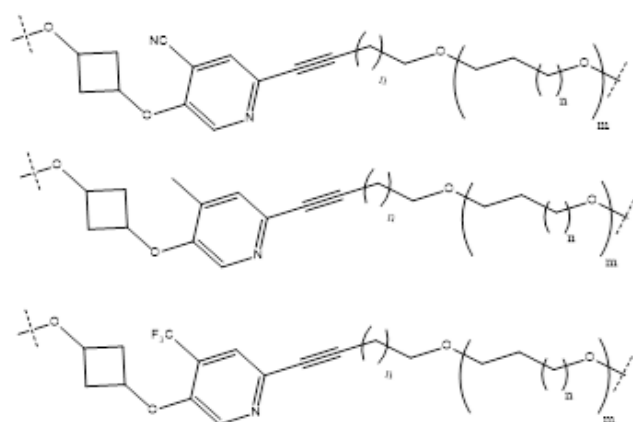
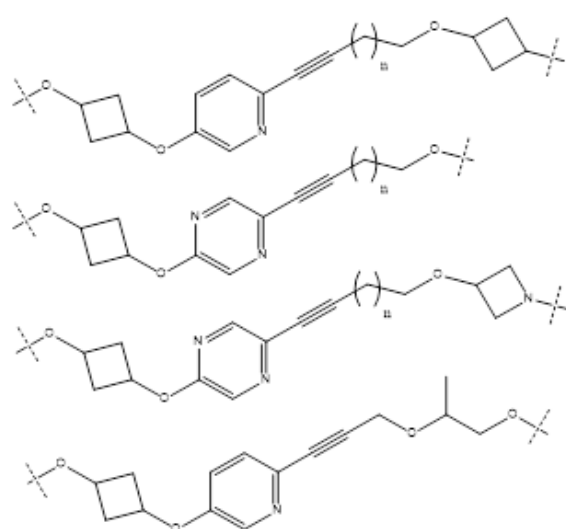
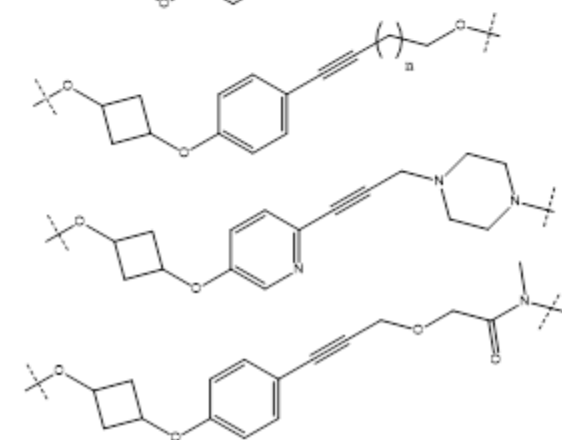
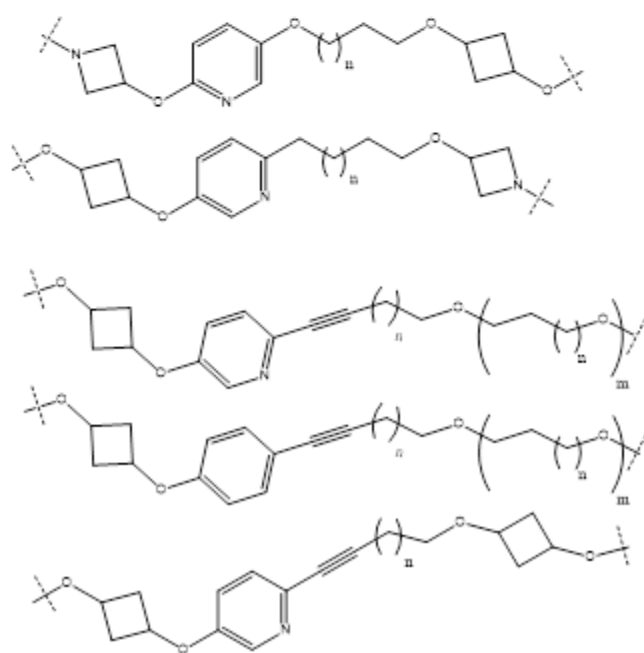
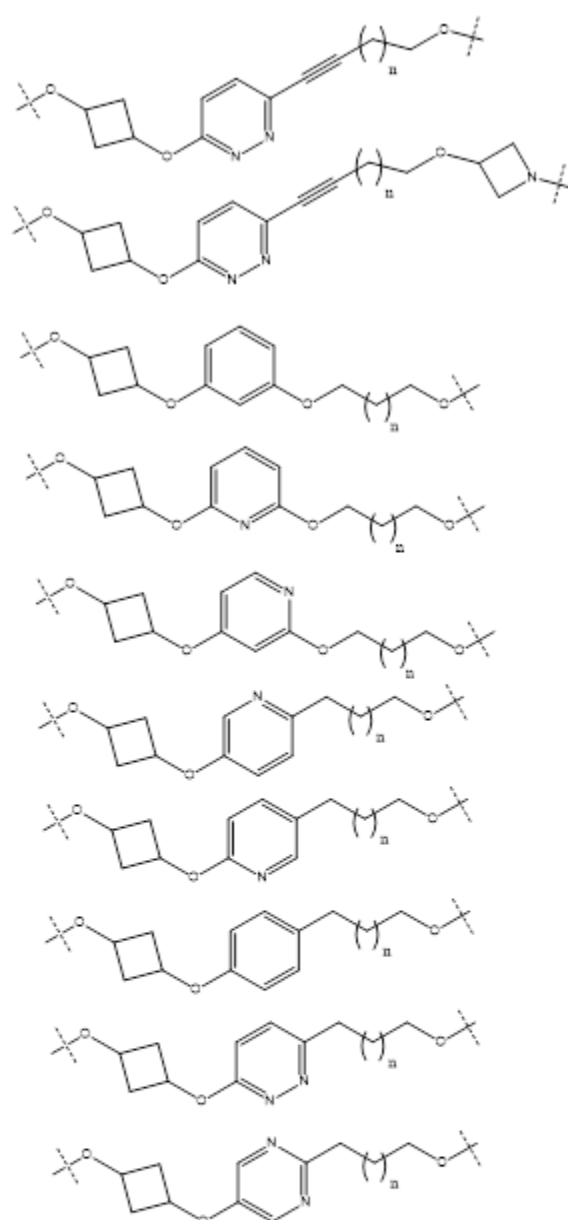
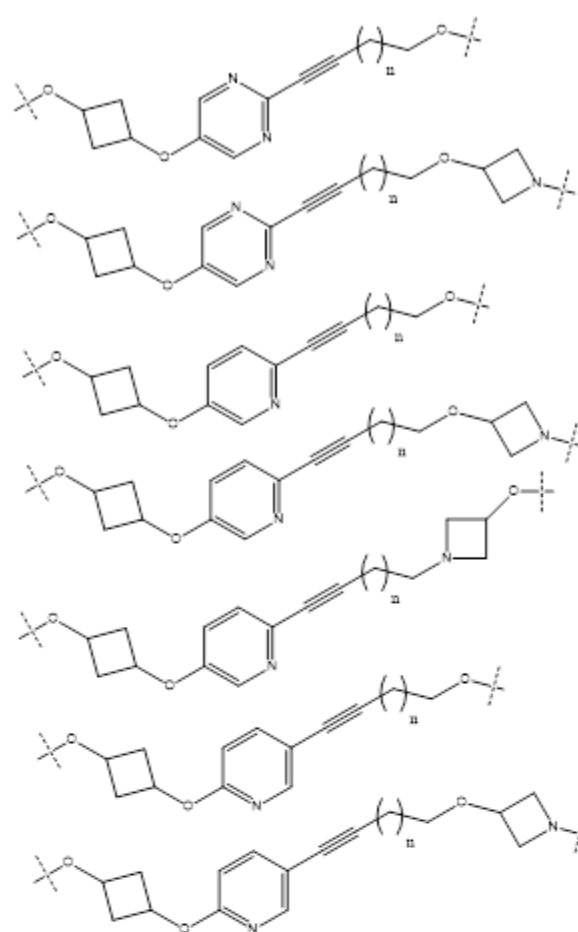
8. El compuesto de conformidad con cualquiera de las reivindicaciones 1 a 5, en donde el enlazador (L) se selecciona del grupo que consiste en:

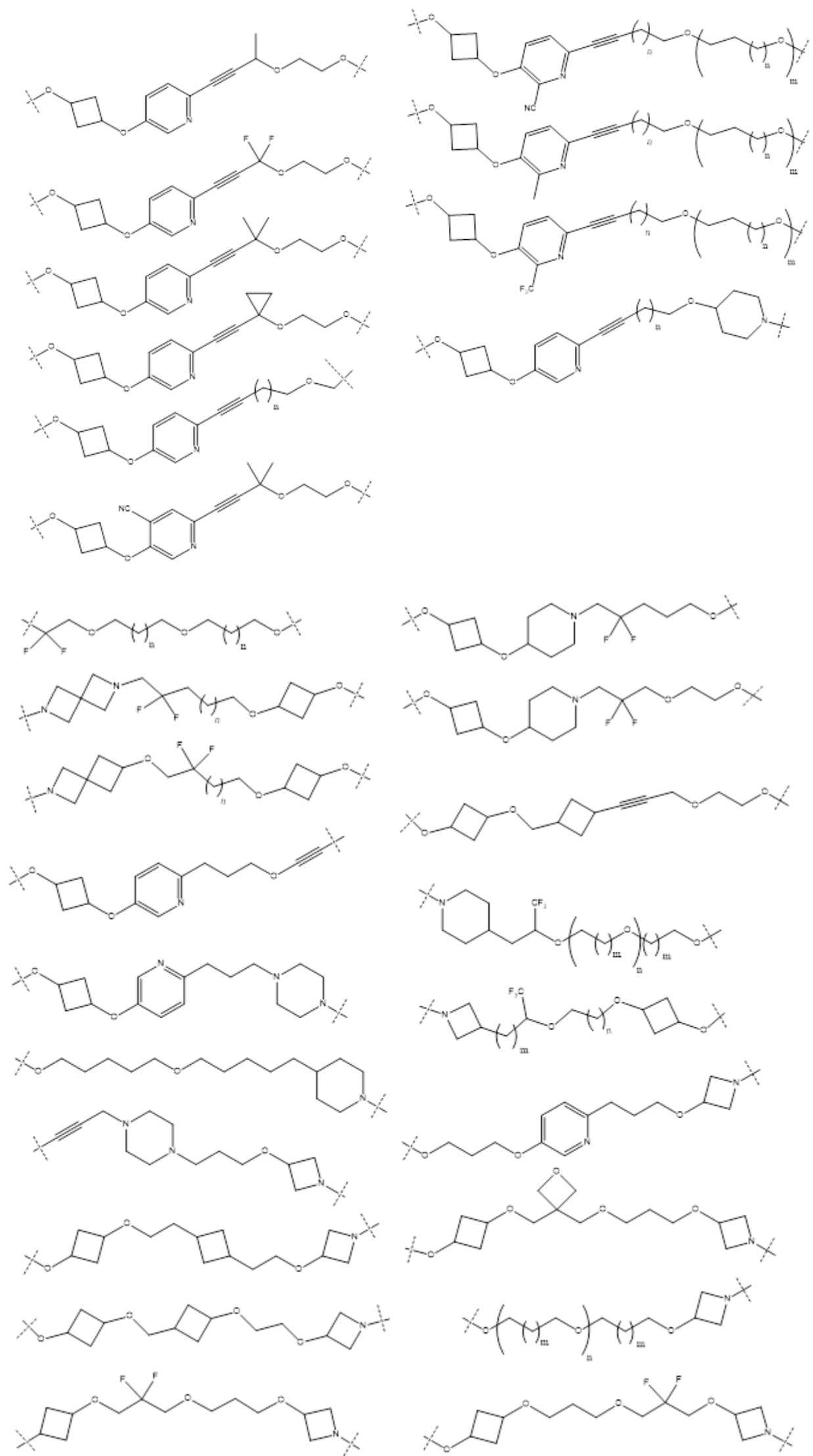


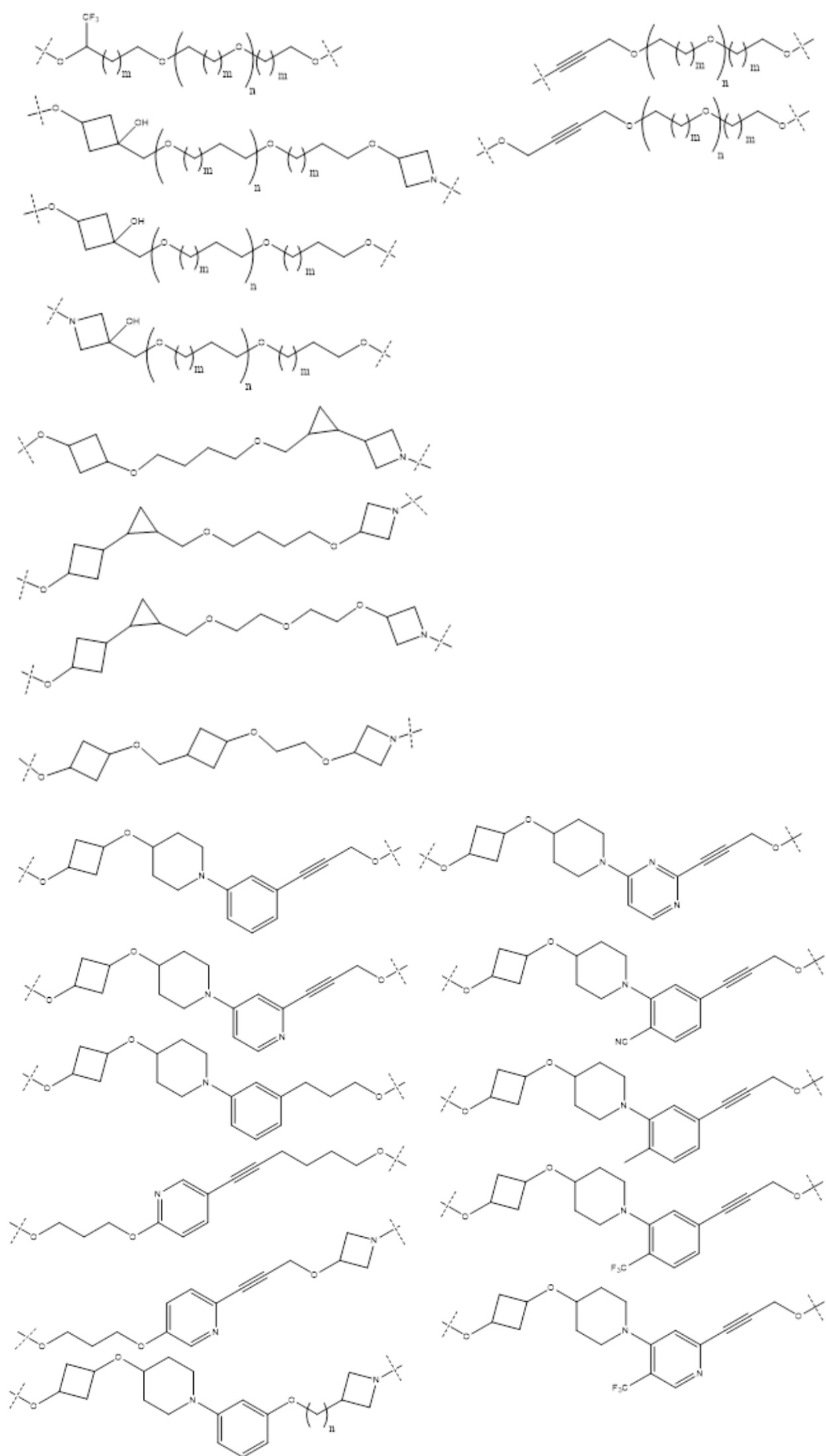


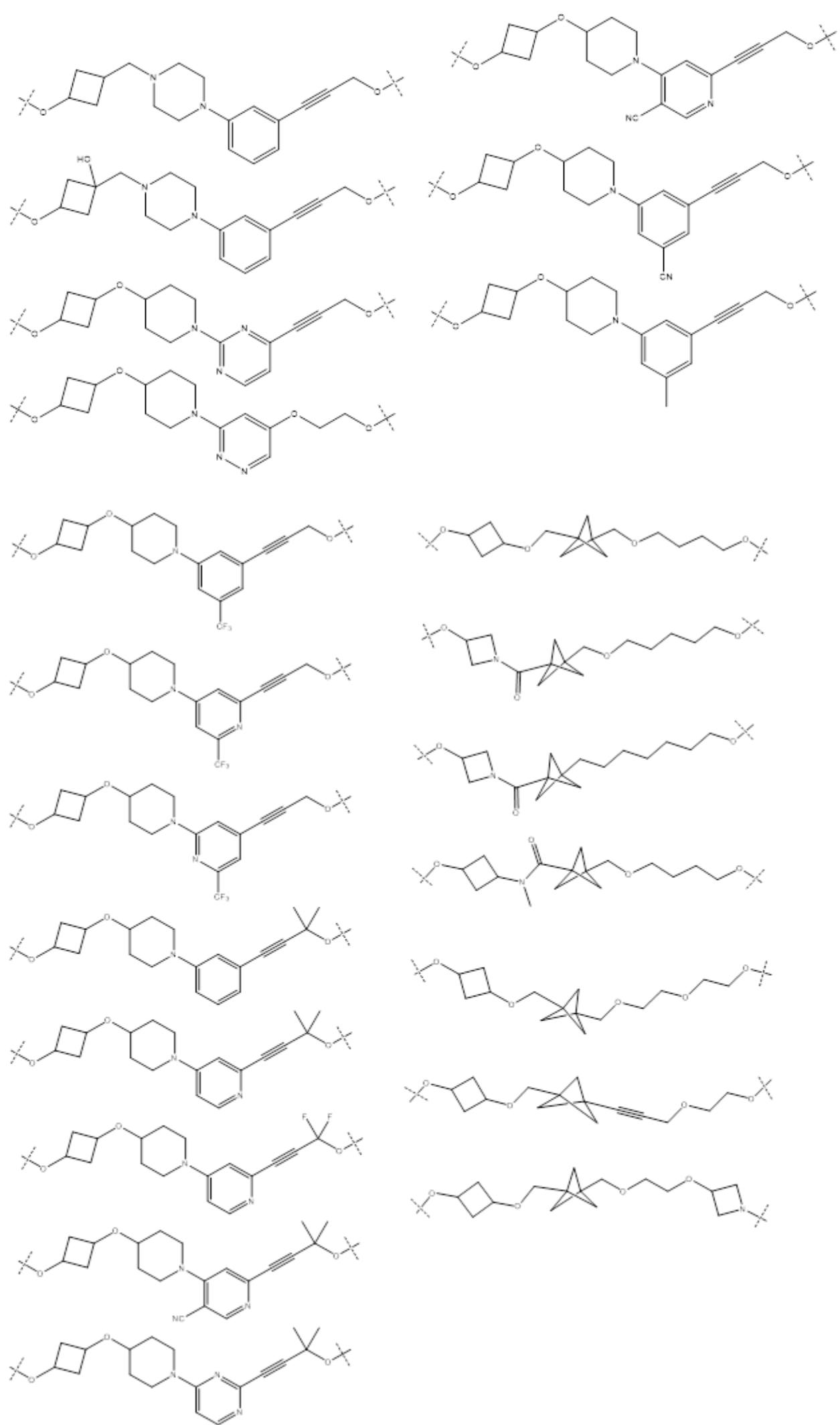


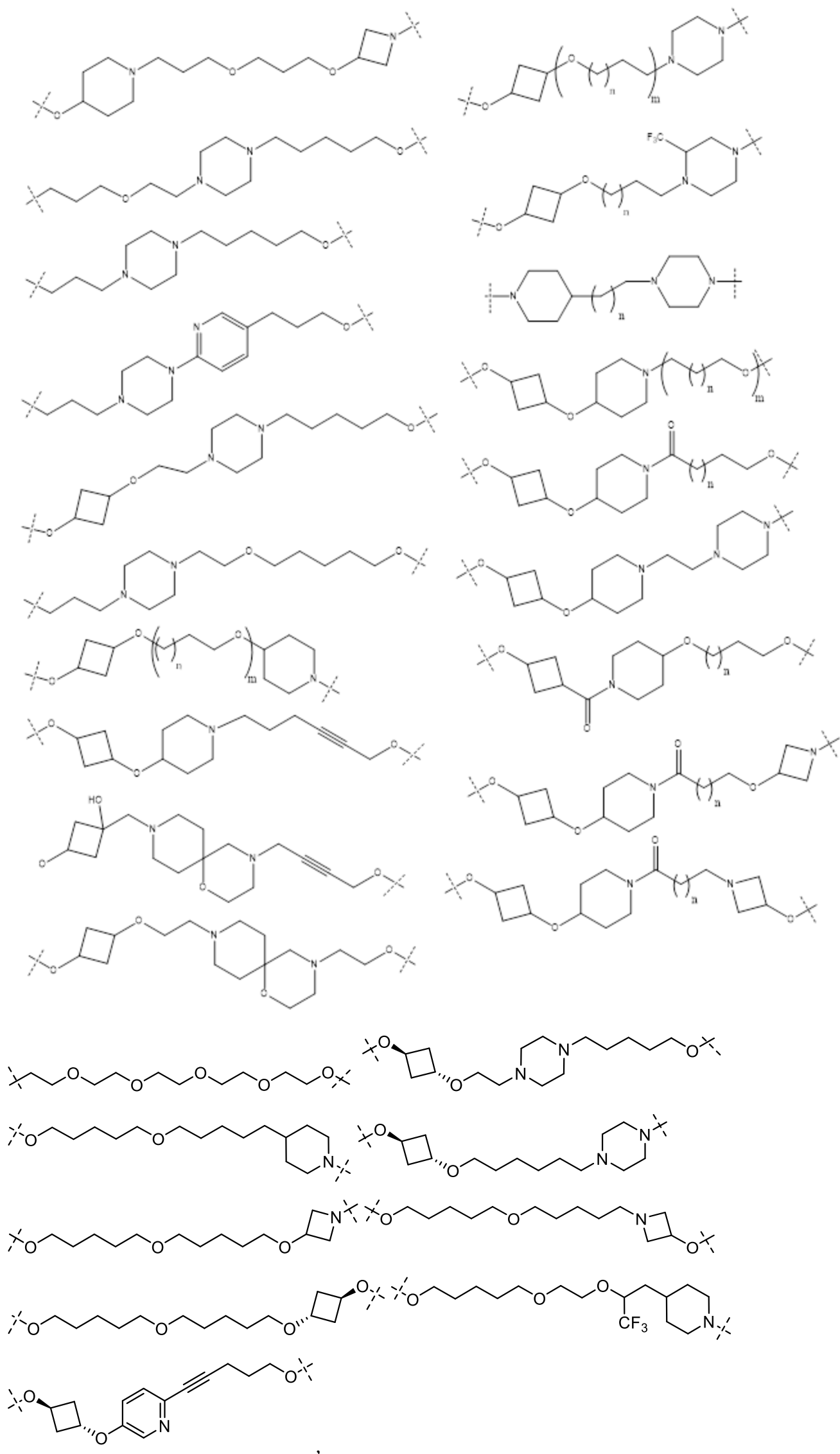






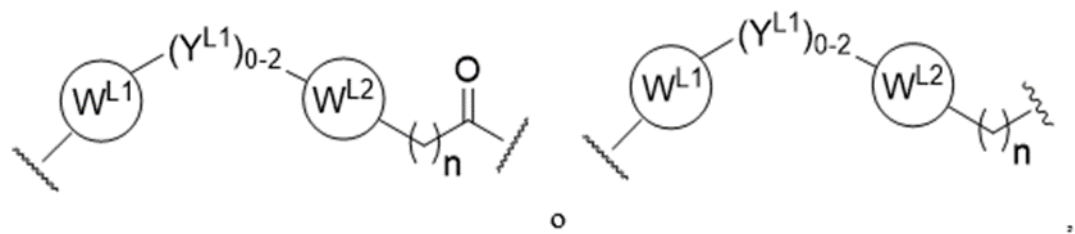






en donde cada n y m es independientemente 0, 1, 2, 3, 4, 5, o 6.

9. El compuesto de conformidad con cualquiera de las reivindicaciones 1 a 5, en donde el L comprende la siguiente estructura química:



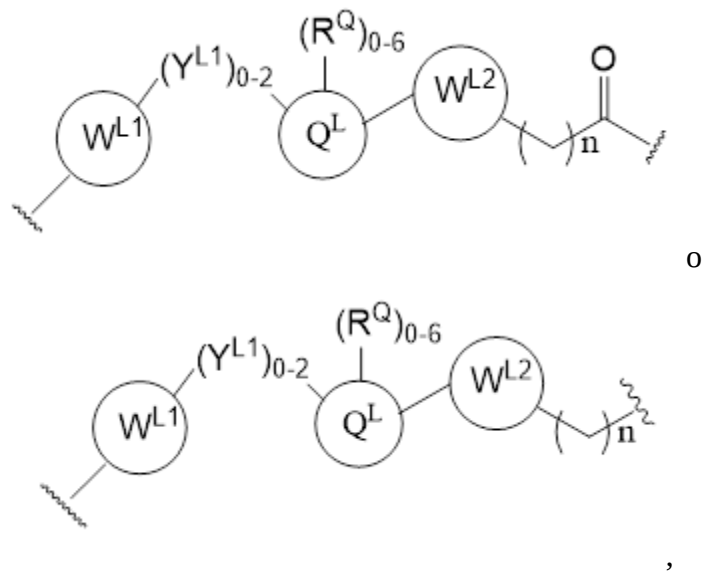
en donde:

$W^{L1}$  y  $W^{L2}$  son cada uno independientemente un anillo de 4-8 miembros con 0-4 heteroátomos, opcionalmente sustituidos con  $R^Q$ , cada  $R^Q$  es independientemente un H, halo, OH, CN,  $CF_3$ , alquilo de C1-C6 (lineal o ramificado), alcoxi de C1-C6 (lineal o ramificado), o 2 grupos  $R^Q$  tomados juntos con el átomo al que se unen para formar un sistema de anillos de 4-8 miembros que contiene 0-4 heteroátomos;

$Y^{L1}$  es cada uno independientemente un enlace, alquilo de C1-C6 lineal o ramificado, opcionalmente sustituido con 1-3 halógenos y opcionalmente uno o más átomos de C se reemplazan con O; o alcoxi de C1-C6 lineal o ramificado, opcionalmente sustituido con 1-3 halógenos; y

una línea discontinua indica el punto de acoplamiento a las porciones PTM o ULM.

10. El compuesto de conformidad con las reivindicaciones 1 a 5, en donde L comprende la siguiente estructura química:



en donde:

$W^{L1}$  y  $W^{L2}$  son cada uno independientemente arilo de C<sub>6-10</sub>, heteroarilo de 6-10 miembros, cicloalquilo de 3-11 miembros, heterocíclico de 3-10 miembros, o alquilo de C<sub>1-6</sub>, cada uno opcionalmente sustituido con  $R^Q$ , cada  $R^Q$  es independientemente un H, halo, OH, CN,  $CF_3$ , hidroxilo, nitro,  $C\equiv CH$ , alquenilo de C<sub>2-6</sub>, alquinilo de C<sub>2-6</sub>, alquilo de C<sub>1-6</sub> lineal o ramificado), alcoxi de C<sub>1-6</sub> (lineal o ramificado),  $OC_{1-3}$ alquilo (opcionalmente sustituido por 1 o más -F), OH,  $NH_2$ ,  $NR^{Y1}R^{Y2}$ , CN, o 2 grupos  $R^Q$  tomados juntos con

el átomo al que se unen para formar un sistema de anillos de 4-8 miembros que contiene 0-4 heteroátomos;

$Y^{L1}$  es cada uno independientemente un enlace,  $NR^{YL1}$ , O, S,  $NR^{YL2}$ ,  $CR^{YL1}R^{YL2}$ , C=O, C=S, SO, SO<sub>2</sub>, C<sub>1</sub>-C<sub>6</sub> alquilo (lineal o ramificado) y opcionalmente uno o más átomos de C se reemplazan con O; C<sub>1</sub>-C<sub>6</sub> alcoxi (lineal, ramificado, opcionalmente sustituido);

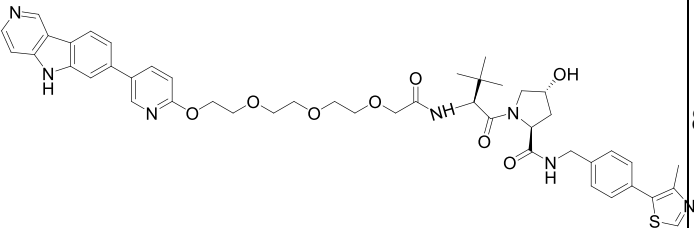
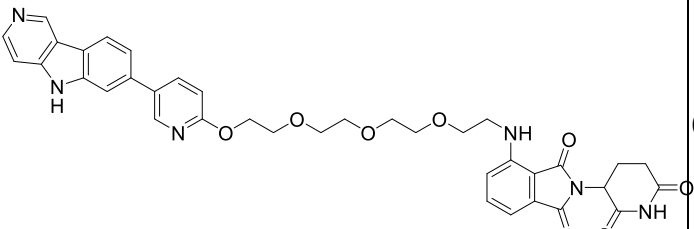
$Q^L$  es un anillo alicíclico o aromático de 3-6 miembros con 0-4 heteroátomos, que opcionalmente establecen puentes, opcionalmente sustituido con 0-6  $R^Q$ , cada  $R^Q$  es independientemente H, o alquilo de C<sub>1-6</sub> lineal o ramificado, opcionalmente sustituido por 1 o más halo o alcoxi de C<sub>1-6</sub>, o 2 grupos  $R^Q$  tomados juntos con el átomo al que se unen para formar un sistema de anillos de 3-8 miembros que contiene 0-2 heteroátomos;

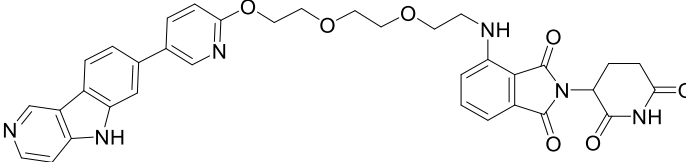
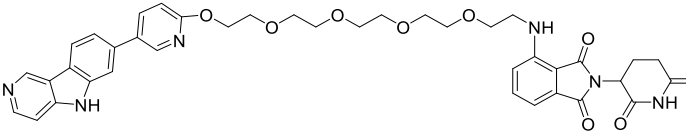
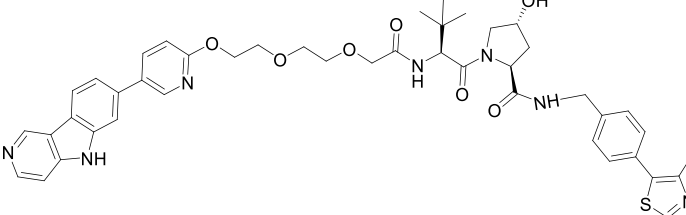
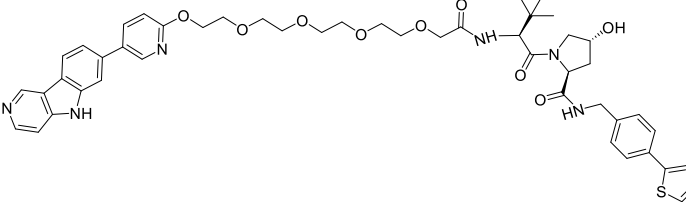
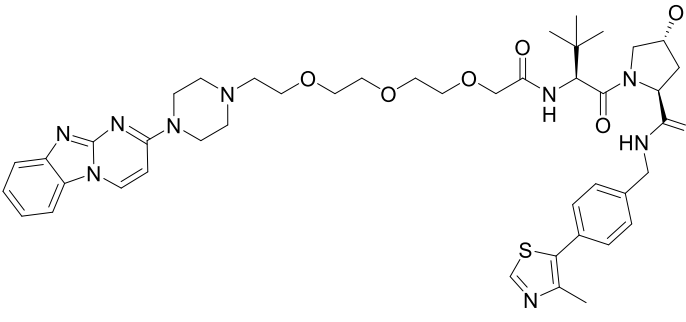
$R^{YL1}$ ,  $R^{YL2}$  son cada uno independientemente H, OH, alquilo de C<sub>1-6</sub> lineal o ramificado, opcionalmente sustituido por 1 o más halo o alcóxido de C<sub>1-6</sub>, o  $R^1$ ,  $R^2$  junto con el átomo al que se unen para formar un sistema de anillos de 3-8 miembros que contiene 0-2 heteroátomos;

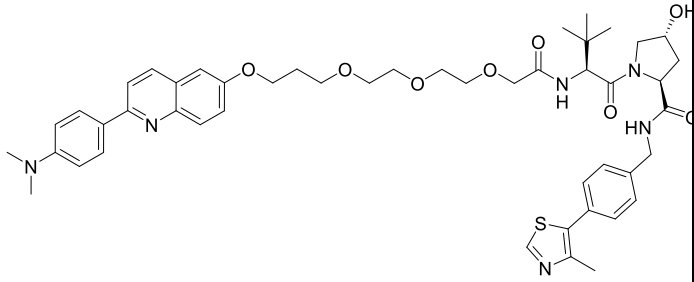
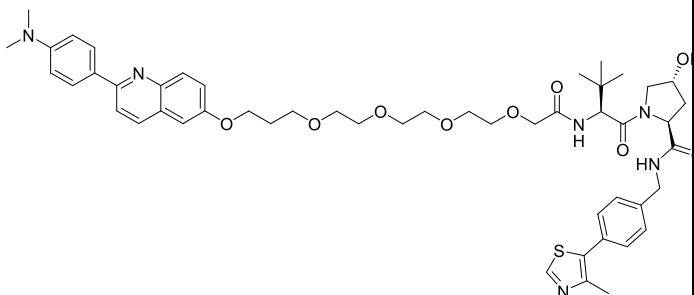
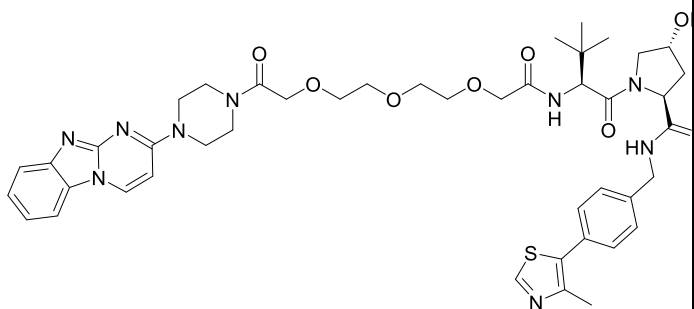
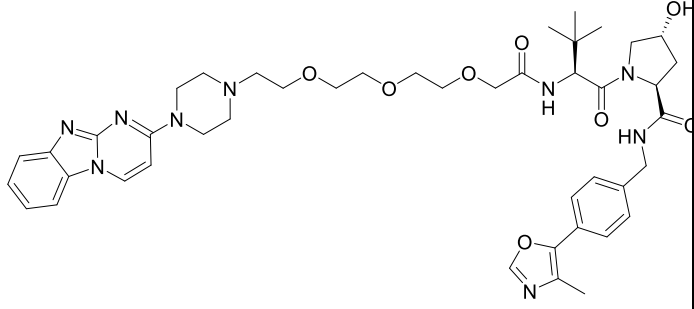
n es 0-10; y

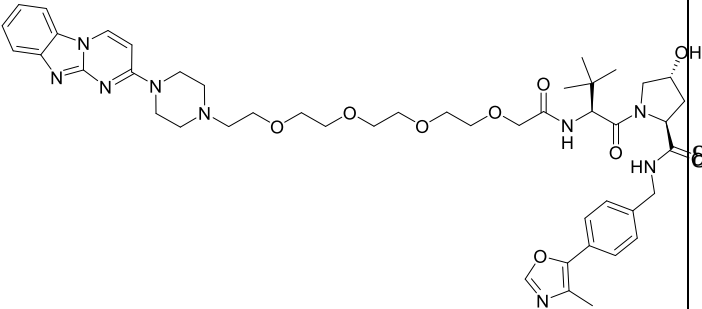
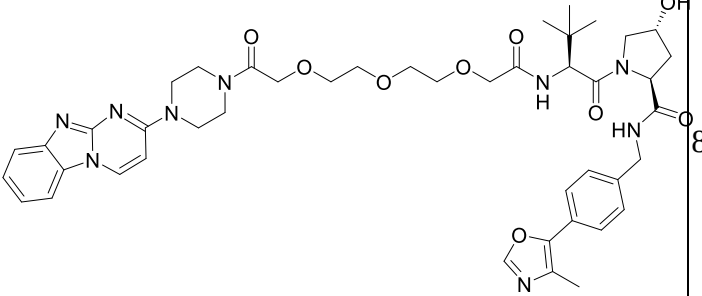
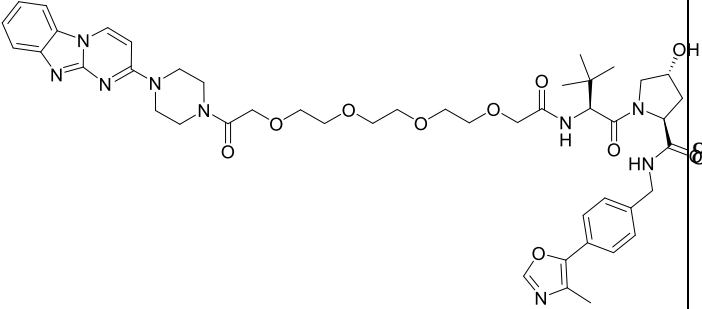
una línea discontinua indica el punto de acoplamiento a las porciones PTM o ULM.

11. El compuesto de conformidad con cualquiera de las reivindicaciones 1 a 5, en donde el L es un grupo polietilenoxi opcionalmente sustituido con arilo de C<sub>6-10</sub> que comprende de 1 a 10 unidades de etilenglicol.
12. El compuesto bifuncional de cualquiera de las reivindicaciones 1 a 11, en donde el compuesto se selecciona del grupo que consiste en los siguientes compuestos:

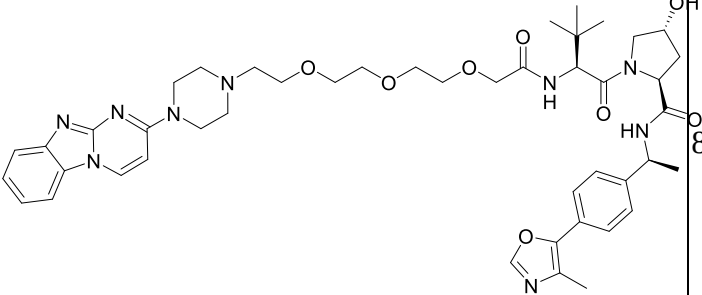
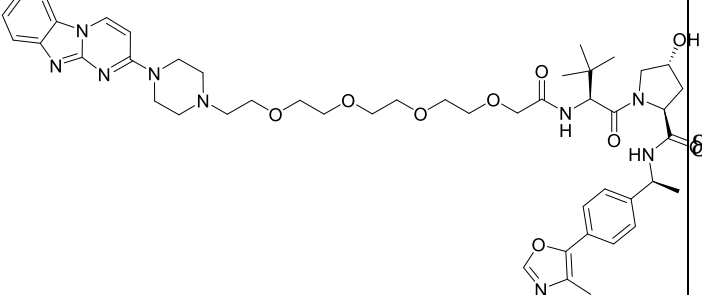
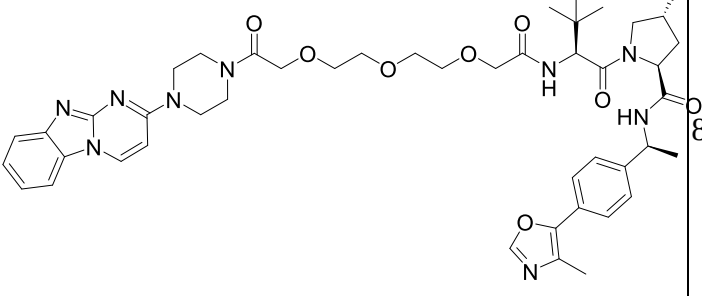
| # | Estructura                                                                          | (M+H) <sup>+</sup> | Datos de NMR                                                                                                                                                                                                                                                                                                                                                                                                                           | Actividad* |
|---|-------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| 1 |  | 864.3              | <sup>1</sup> HNMR (400 MHz, MeOD) : δ 9.39 (s, 1H), 8.82 (s, 1H), 8.47-8.45 (m, 2H), 8.33 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 6.4 Hz, 1H), 7.81 (s, 1H), 7.73 (d, J = 6.0 Hz, 1H), 7.63 (d, J = 6.0 Hz, 1H), 7.43-7.36 (m, 4H), 6.92 (d, J = 8.4 Hz, 1H), 4.78 (s, 1H), 4.69-4.50 (m, 5H), 4.43-4.31 (m, 1H), 4.04-4.02 (m, 2H), 3.87-3.85 (m, 3H), 3.73-3.64 (m, 9H), 2.40 (s, 3H), 2.25-2.19 (m, 1H), 2.15-2.10 (m, 1H), 1.03 (s, 9H). | C          |
| 2 |  | 693.3              | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 9.29 (s, 2H), 8.52-8.51 (m, 1H), 8.50 (s, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.54 (s, 1H), 7.50-7.35 (m, 3H), 6.96 (d, J = 7.2 Hz, 1H),                                                                                                                                                                                                                      | A          |

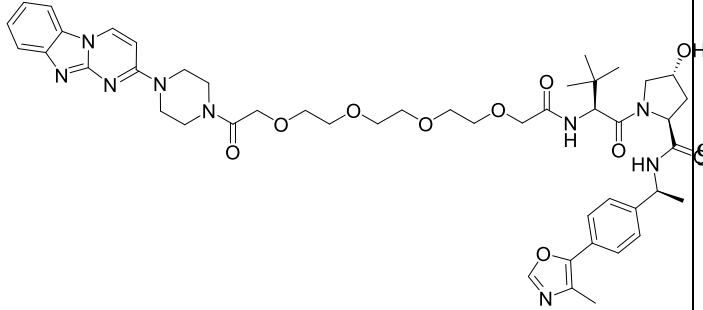
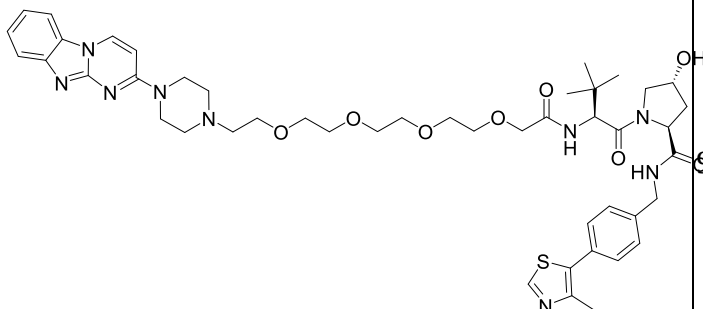
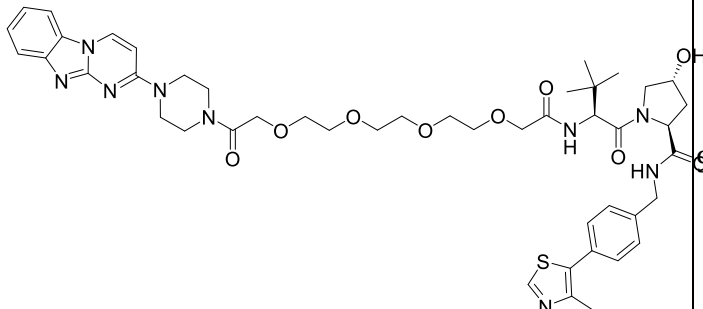
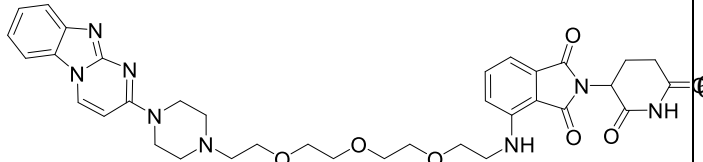
|   |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |   |
|---|-------------------------------------------------------------------------------------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
|   |                                                                                     |       | 6.83-6.81 (m, 2H), 6.39 (s, 1H), 4.93-4.91(m, 1H), 4.53 (s, 2H), 3.88 (s, 2H), 3.72-3.3.60 (m,10H), 3.40-3.30 (m, 2H), 2.88-2.70 (m, 3H), 2.15-2.10(m, 1H).                                                                                                                                                                                                                                                                                                                                     |   |
| 3 |    | 649.3 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 9.32 (s, 1H), 8.67(s, 1H), 8.46-8.54 (m, 2H), 8.15 (d, <i>J</i> = 8.0 Hz, 1H), 7.87(d, <i>J</i> = 8.0 Hz, 1H), 7.58 (s, 1H), 7.35-7.47 (m, 2H), 7.26 (s, 1H), 6.85-6.99 (m, 3H), 6.48 (s, 1H), 4.92 (m, 1H), 4.56-4.58 (m, 2H), 3.93 (s, 2H), 3.41-3.77 (m, 9H), 2.71-2.85 (m, 3H), 2.02 (s, 1H).                                                                                                                                           | A |
| 4 |  | 737.4 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 9.30 (s, 1H), 8.90(br, 1H), 8.52 (d, <i>J</i> = 5.6 Hz,1H), 8.42 (d, <i>J</i> = 2,8 Hz, 1H), 8.14(d, <i>J</i> = 8.0 Hz ,1H), 7.49 (dd, <i>J</i> = 2.4, 8.8 Hz, 1H), 7.57 (s, 1H), 7.26-7.46 (m, 3H), 6.97 (d, <i>J</i> = 7.2 Hz, 1H), 6.81-6.87 (m, 2H), 6.35-6.46 (m, 1H), 4.89-4.98 (m, 1H), 4.54 (t, <i>J</i> = 4.8 Hz, 2H), 3.90 (t, <i>J</i> = 4.8 Hz, 2H), 3.61-3.74 (m, 15H), 3.37-3.81 (m, 2H), 2.65-2.92(m, 3H), 2.07-2.15(m, 1H). | A |
| 5 |  | 820.4 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | C |
| 6 |  | 908.4 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | C |
| 7 |  | 856.5 | <sup>1</sup> H NMR (400MHz, MeOD): δ 8.85 (s, 1H), 8.71 (d, <i>J</i> = 7.6 Hz, 1H), 7.70 (d, <i>J</i> = 8.0 Hz, 1H), 7.55 (d, <i>J</i> = 8.0 Hz, 1H), 7.34-7.42 (m, 5H), 7.22-7.23 (m, 1H), 6.76 (d, <i>J</i> = 7.6 Hz, 1H), 4.68 (s, 1H), 4.47-4.57 (m, 4H), 4.30-4.39 (m, 1H), 4.05 (s, 3H), 3.56-4.87 (m, 23H), 2.64(s, 4H), 2.45 (s, 3H),                                                                                                                                                   | C |

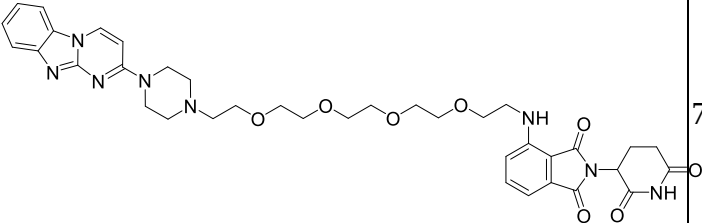
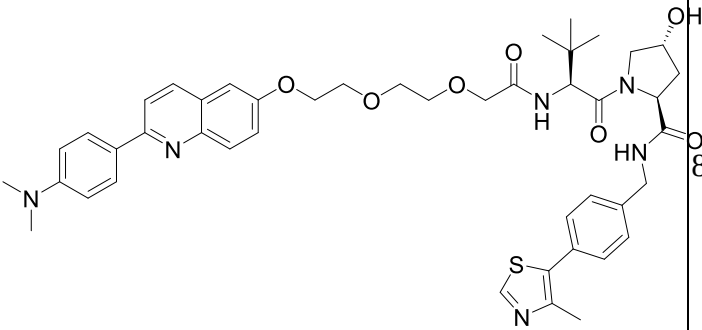
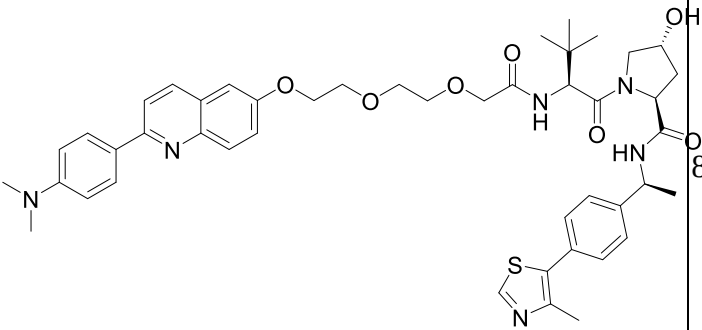
|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |
|----|-------------------------------------------------------------------------------------|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
|    |                                                                                     |       | 2.19 (br, 1H), 2.04 (br, 1H), 1.03 (s, 9H).                                                                                                                                                                                                                                                                                                                                                                                                         |   |
| 8  |    | 881.6 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.02 (s, 9H), 2.07-2.25 (m, 4H), 2.46 (s, 3H), 3.04 (s, 6H), 3.65-3.71 (m, 10H), 3.78-3.86 (m, 2H), 4.01-4.06 (m, 2H), 4.18-4.21 (m, 2H), 4.32-4.36 (m, 1H), 4.50-4.60 (m, 3H), 4.68-4.70 (m, 1H), 6.88 (d, <i>J</i> = 9.2 Hz, 2H), 7.23-7.26 (m, 1H), 7.34-7.44 (m, 5H), 7.82 (d, <i>J</i> = 8.4 Hz, 1H), 7.92-7.96 (m, 3H), 8.16 (d, <i>J</i> = 8.8 Hz, 1H), 8.86 (s, 1H).                     | C |
| 9  |  | 925.6 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.04 (s, 9H), 2.08-2.12 (m, 3H), 2.20-2.23 (m, 1H), 2.46 (s, 3H), 3.04 (s, 6H), 3.62-3.71 (m, 14H), 3.78-3.89 (m, 2H), 4.01-4.19 (m, 2H), 4.14-4.23 (m, 2H), 4.33-4.37 (m, 1H), 4.51-4.58 (m, 3H), 4.68-4.70 (m, 1H), 6.68 (d, <i>J</i> = 8.4 Hz, 1H), 7.24 (br, 1H), 7.36-7.45 (m, 5H), 7.62-7.64 (m, 1H), 7.79-7.84 (m, 1H), 7.93-7.97 (m, 3H), 8.17 (d, <i>J</i> = 8.0 Hz, 1H), 8.68 (s, 1H). | C |
| 10 |  | 870.5 | <sup>1</sup> H NMR (400MHz, MeOD): δ 8.85 (s, 1H), 8.77 (d, <i>J</i> = 8.0 Hz, 1H), 7.83 (d, <i>J</i> = 8.0 Hz, 1H), 7.57 (d, <i>J</i> = 8.0 Hz, 1H), 7.37-7.45 (m, 5H), 7.25 (t, <i>J</i> = 8.0 Hz, 1H), 6.79 (d, <i>J</i> = 8.0 Hz, 1H), 4.68 (s, 1H), 4.49-4.60 (m, 3H), 4.24-4.36 (m, 3H), 4.01-4.06 (m, 2H), 3.91-3.98 (m, 2H), 3.86-3.89 (m, 2H), 3.65-3.80 (m, 14H), 2.45 (s, 3H), 2.20-2.26 (m, 1H), 2.04-2.11 (m, 1H), 1.03 (s, 9H).       | C |
| 11 |  | 840.6 | <sup>1</sup> H NMR (400 MHz, MeOD): δ 8.70 (d, <i>J</i> = 7.6 Hz, 1H), 8.11 (s, 1H), 7.80 (d, <i>J</i> = 8.4 Hz, 1H), 7.53-7.55 (m, 3H), 7.43 (d, <i>J</i> = 8.4 Hz, 2H), 7.37 (t, <i>J</i> = 8.0 Hz, 2H), 7.23 (d, <i>J</i> = 7.6 Hz, 1H), 6.76 (d, <i>J</i> = 7.6 Hz, 1H), 4.84 (s, 1H), 4.53-4.60 (m, 1H), 4.49 (s, 1H), 4.31-                                                                                                                   | C |

|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                             |   |
|----|-------------------------------------------------------------------------------------|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
|    |                                                                                     |       | 4.35 (m, 1H), 4.05 (s, 2H), 3.77–3.80 (m 5H), 3.65–3.70 (m, 10H), 2.64–2.66 (m, 6H), 2.36 (s, 3H), 2.11–2.20 (m, 1H), 2.04–2.10 (m, 1H), 1.04 (s, 9H).                                                                                                                                                                                                                                                                      |   |
| 12 |   | 884.4 | <sup>1</sup> H NMR (400 MHz, MeOD): δ 8.71 (br, 1H), 8.12 (s, 1H), 7.80–7.82 (m, 1H), 7.43–7.56 (m, 3H), 7.35–7.39 (m, 3H), 7.24–7.25 (m, 1H), 6.76–6.78 (m, 1H), 4.49 (s, 1H), 4.54–4.58 (m, 3H), 4.32–4.36 (m, 1H), 4.04 (s, 1H), 3.81–3.92 (m, 5H), 3.61–3.69 (m, 12H), 3.35 (s 1H), 2.66–2.75 (m, 6H), 2.37 (s, 3H), 2.20–2.22(m, 1H), 2.07–2.15 (m, 1H), 1.04 (s, 9H).                                                 | C |
| 13 |  | 854.5 | <sup>1</sup> H NMR (400MHz, MeOD): δ 8.79 (d, <i>J</i> = 7.6 Hz, 1H), 8.12 (s, 1H), 7.85 (d, <i>J</i> = 8.0 Hz, 1H), 7.54–7.58 (m, 3H), 7.39–7.43 (m, 2H), 7.28 (t, <i>J</i> = 7.6 Hz, 1H), 6.83 (d, <i>J</i> = 8.0 Hz, 1H), 4.68 (s, 1H), 4.67 (s, 1H), 4.55–4.61 (m, 1H), 4.44 (br, 1H), 4.29–4.35 (m, 5H), 3.80–4.03 (m, 8H), 3.71–3.82 (m, 13H), 3.37 (s, 3H), 2.20–2.22 (s, 1H), 2.08–2.10 (m, 1H), 1.04 (s, 9H).      | C |
| 14 |  | 898.6 | <sup>1</sup> H NMR (400 MHz, MeOD): δ 8.76 (d, <i>J</i> = 7.2 Hz, 1H), 8.09 (s, 1H), 7.84 (d, <i>J</i> = 7.2 Hz, 1H), 7.35–7.63 (m, 6H), 7.28 (t, <i>J</i> = 7.6 Hz, 1H), 6.82 (d, <i>J</i> = 7.6 Hz, 1H), 4.68 (s, 1H), 4.50–4.61 (m, 3H), 4.28–4.39 (m, 3H), 4.06 (s, 2H), 3.86–3.97 (m, 3H), 3.78–3.81 (m, 1H), 3.55–3.76 (m, 16H), 3.18–3.23 (m, 2H), 2.35 (s, 3H), 2.21–2.26 (m, 1H), 2.04–2.10 (m, 1H), 1.04 (s, 9H). | C |

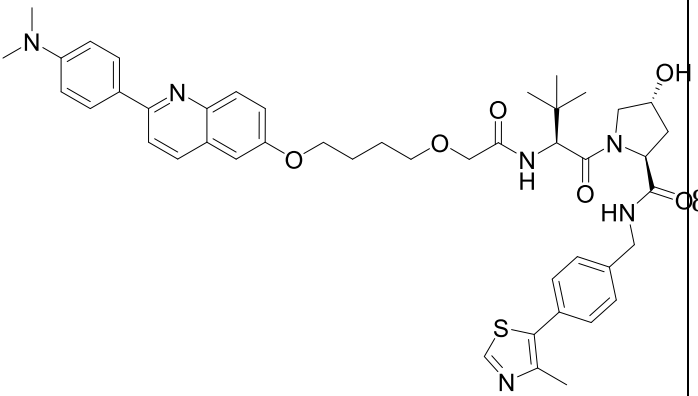
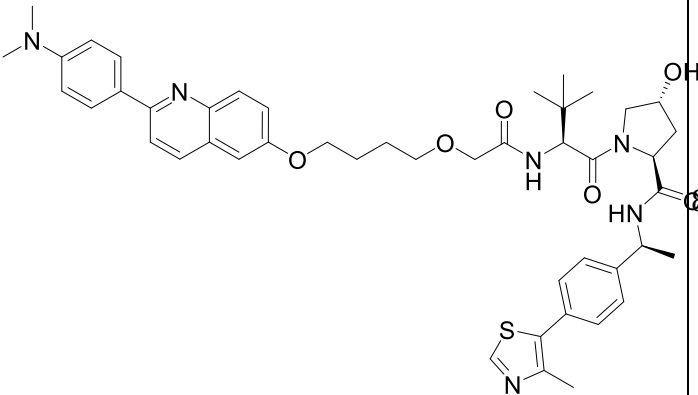
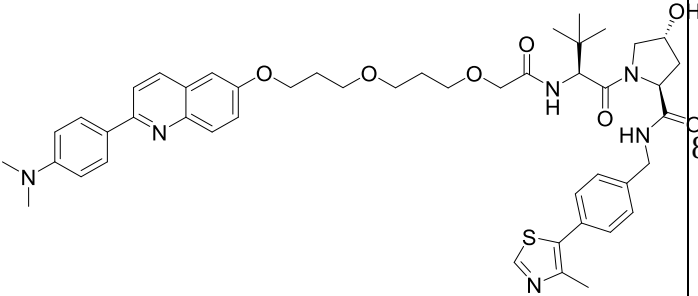
|    |  |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |   |
|----|--|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
| 15 |  | 870.6 | <sup>1</sup> H NMR (400 MHz, MeOD): $\delta$ 8.85 (s, 1H), 8.76 (d, $J$ = 8.0 Hz, 1H), 7.83 (d, $J$ = 8.0 Hz, 1H), 7.56 (d, $J$ = 7.6 Hz, 1H), 7.37–7.40 (m, 6H), 7.26 (t, $J$ = 7.2 Hz, 1H), 6.84 (d, $J$ = 8.0 Hz, 1H), 4.99–5.01 (m, 1H), 4.68 (s, 1H), 4.57 (t, $J$ = 7.6 Hz, 1H), 4.44 (s, 1H), 4.05 (br, 2H), 3.83–3.91 (m, 5H), 3.68–3.76 (m, 12H), 2.70 (m, 6H), 2.45 (s, 3H), 2.17–2.20 (m, 1H), 1.96–2.05 (m, 1H), 1.56 (d, $J$ = 7.2 Hz, 3H), 1.05 (s, 9H). | C |
| 16 |  | 914.6 | <sup>1</sup> H NMR (400 MHz, MeOD): $\delta$ 8.80–8.85 (m, 2H), 7.88 (d, $J$ = 8.0 Hz, 1H), 7.57 (d, $J$ = 8.0 Hz, 1H), 7.32–7.46 (m, 7H), 6.93 (d, $J$ = 8.0 Hz, 1H), 4.99–5.01 (m, 1H), 4.68 (s, 1H), 4.55–4.57 (m, 1H), 4.43 (s, 1H), 4.04 (s, 2H), 3.80–3.94 (m, 4H), 3.83–3.85 (m, 15H), 2.72–2.74 (m, 6H), 2.46 (s, 3H), 2.12–2.13 (m, 1H), 1.97–1.99 (m, 1H), 1.96–2.05 (m, 1H), 1.56 (d, $J$ = 7.2 Hz, 3H), 1.05 (s, 9H).                                      | C |
| 17 |  | 884.5 | <sup>1</sup> H NMR (400 MHz, MeOD): $\delta$ 8.85 (s, 1H), 8.78 (d, $J$ = 7.6 Hz, 1H), 7.83 (d, $J$ = 7.6 Hz, 1H), 7.57 (d, $J$ = 7.6 Hz, 1H), 7.35–7.40 (m, 6H), 7.23 (t, $J$ = 8.0 Hz, 1H), 4.98–5.00 (m, 1H), 4.67 (s, 1H), 4.55–4.57 (m, 1H), 4.34–4.43 (m, 3H), 3.83–4.03 (m, 7H), 3.72–3.74 (m, 16H), 2.46 (s, 3H), 2.17–2.21 (m, 1H), 1.95–2.10 (m, 1H), 1.31 (d, $J$ = 8.8 Hz, 3H), 1.03 (s, 9H).                                                              | C |
| 18 |  | 928.7 | <sup>1</sup> H NMR (400 MHz, MeOD): $\delta$ 8.75–8.86 (m, 2H), 7.85 (d, $J$ = 8.0 Hz, 1H), 7.56 (d, $J$ = 8.0 Hz, 1H), 7.34–7.42 (m, 5H), 7.27 (t, $J$ = 7.6 Hz, 1H), 6.79–6.85 (m, 1H), 4.94–5.04 (m, 1H), 4.67 (s, 1H), 4.55–4.61 (m, 1H), 4.44 (br, 1H), 4.29–4.35 (m, 2H), 4.07 (s, 2H), 3.83–3.96 (m, 4H), 3.61–                                                                                                                                                 | C |

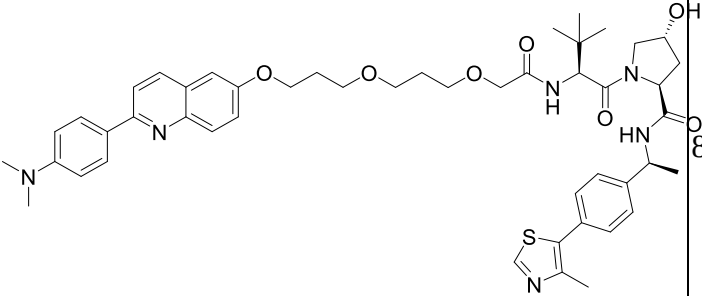
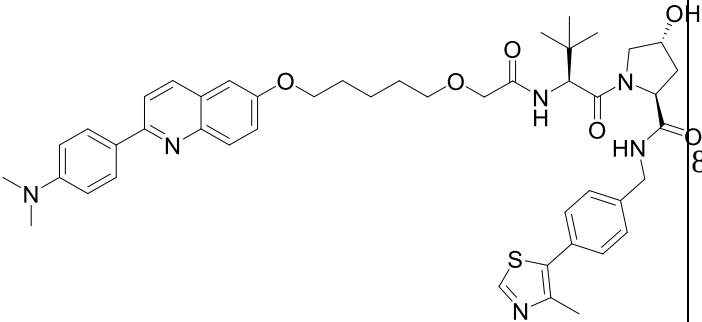
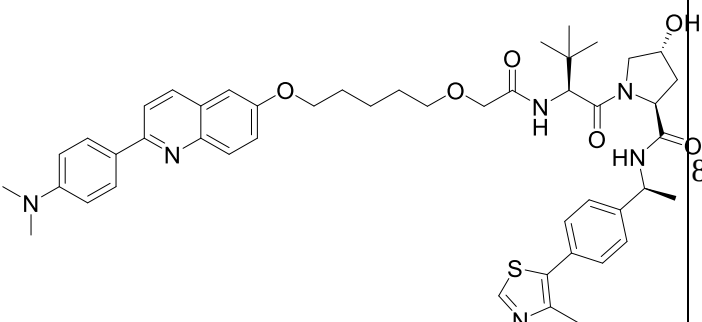
|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |
|----|-------------------------------------------------------------------------------------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
|    |                                                                                     |       | 3.79 (m, 16H), 3.18–3.23 (m, 2H), 2.45 (s, 3H), 2.18–2.23 (m, 1H), 1.92–1.99 (m, 1H), 1.48–1.57 (m, 3H), 1.03 (s, 9H).                                                                                                                                                                                                                                                                                                                                                              |   |
| 19 |    | 854.6 | <sup>1</sup> H NMR (400 MHz, MeOD): $\delta$ 8.76 (d, $J$ = 7.6 Hz, 1H), 8.11 (s, 1H), 7.84 (d, $J$ = 8.0 Hz, 1H), 7.56 (t, $J$ = 8.4 Hz, 3H), 7.40 (d, $J$ = 8.4 Hz, 3H), 7.27 (t, $J$ = 8.0 Hz, 1H), 6.85 (m, $J$ = 7.6 Hz, 1H), 4.98–4.50 (m, 1H), 4.75 (s, 1H), 4.57 (t, $J$ = 7.6 Hz, 1H), 4.43 (s, 1H), 4.05 (s, 2H), 3.83–3.91 (m, 5H), 3.67–3.76 (m, 12H), 2.70–2.71 (m, 6H), 2.37 (s, 3H), 2.17–2.19 (m, 1H), 1.95–2.10 (m, 1H), 1.55 (d, $J$ = 6.4 Hz, 3H), 1.05 (s, 9H). | C |
| 20 |  | 898.6 | <sup>1</sup> H NMR (400 MHz, MeOD): $\delta$ 8.72 (d, $J$ = 8.0 Hz, 1H), 8.11 (s, 1H), 7.81 (d, $J$ = 8.0 Hz, 1H), 7.54–7.56 (m, 3H), 7.35–7.41 (m, 3H), 7.24 (t, $J$ = 8.0 Hz, 1H), 6.79 (d, $J$ = 8.0 Hz, 1H), 4.96–4.50 (m, 1H), 4.68 (s, 1H), 4.55–4.59 (m, 1H), 4.43 (s, 1H), 4.04 (s, 2H), 3.74–3.89 (m, 5H), 3.68–3.70 (m, 18H), 2.68–2.72 (m, 6H), 2.37 (s, 3H), 2.17–2.19 (m, 1H), 1.95–2.10 (m, 1H), 1.50 (d, $J$ = 6.4 Hz, 3H), 1.04 (s, 9H).                            | C |
| 21 |  | 868.3 | <sup>1</sup> H NMR (400 MHz, MeOD): $\delta$ 8.77 (d, $J$ = 8.0 Hz, 1H), 8.12 (s, 1H), 7.82 (d, $J$ = 8.0 Hz, 1H), 7.56–7.58 (m, 3H), 7.35–7.41 (m, 3H), 7.23 (d, $J$ = 8.0 Hz, 1H), 6.79 (d, $J$ = 7.6 Hz, 1H), 4.98–4.99 (m, 1H), 4.67 (s, 1H), 4.55–4.59 (m, 1H), 4.43 (s, 1H), 4.33–4.35 (m, 2H), 3.86–4.01 (m, 7H), 3.72–3.74 (m, 14H), 2.38 (s, 3H), 2.17–2.19 (m, 1H), 1.95–2.05 (m, 1H), 1.48 (d, $J$ = 6.8 Hz, 3H), 1.03 (s, 9H).                                          | C |

|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                            |   |
|----|-------------------------------------------------------------------------------------|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
| 22 |    | 912.6 | <sup>1</sup> H NMR (400 MHz, MeOD): δ 8.75–8.81 (m, 1H), 8.06–8.10 ( m, 1H), 7.86 (d, <i>J</i> = 8.0 Hz, 1H), 7.55–7.61 (m, 3H), 7.35–7.43 (m, 3H), 7.25–7.31 (m, 1H), 6.81–6.88 (m, 1H), 4.94–5.04 (m, 1H), 4.67 (s, 1H), 4.55–4.60 (m, 1H), 4.43 (br, 1H), 4.35 (s, 2H), 4.07 (s, 2H), 3.91–3.97 (m, 3H), 3.82–3.85 (m, 1H), 3.61–3.79 (m, 16H), 3.18–3.23 (m, 2H), 2.37 (s, 3H), 2.18–2.23 (m, 1H), 1.92–1.99 (m, 1H), 1.48–1.56 (m, 3H), 1.04 (s, 9H). | C |
| 23 |   | 900.6 | <sup>1</sup> H NMR (400 MHz, MeOD): δ 8.85 (s, 1H), 8.70 (d, <i>J</i> = 8.0 Hz, 1H), 7.79 (d, <i>J</i> = 8.0 Hz, 1H), 7.54 (d, <i>J</i> = 8.0 Hz, 1H), 7.34-7.44 (m, 5H), 7.24 (t, <i>J</i> = 6.8 Hz, 4.8 Hz, 1H), 6.75 (d, <i>J</i> = 8.0 Hz, 1H), 4.69 (s, 1H), 4.57 (m, 3H), 4.50 (d, <i>J</i> = 4.8 Hz, 1H), 4.04 (s, 2H), 3.85 (s, 6H), 3.60-3.69 (m, 15H), 2.66 (s, 6H), 2.65 (s, 3H), 2.08-2.45 (m, 2H), 2.28 (s, 2H), 1.04 (s, 9H).                | C |
| 24 |  | 914.6 | <sup>1</sup> H NMR (400MHz, MeOD): δ 8.84 (s, 1H), 8.77 (d, <i>J</i> = 8.0 Hz, 1H), 8.83 (d, <i>J</i> = 8.0 Hz, 1H), 7.57 (d, <i>J</i> = 8.0 Hz, 1H), 7.37-7.45 (m, 5H), 7.24-7.28 (m, 1H), 6.81 (d, <i>J</i> = 8.0 Hz, 1H), 4.86 (s, 1H), 4.50-4.63 (m, 3H), 4.26-4.36 (m, 3H), 3.91-4.03 (m, 4H), 3.86-3.89 (m, 2H), 3.74-3.81(m, 2H), 3.60-3.72(m, 16H), 2.45 (s, 3H), 2.18-2.26 (m, 1H), 2.05-2.11 (m, 1H), 1.03 (s, 9H).                              | C |
| 25 |  | 685.4 | <sup>1</sup> H NMR (400MHz, MeOD): δ 8.68 (d, <i>J</i> = 8.0 Hz, 1H), 7.80 (d, <i>J</i> = 7.2 Hz, 1H), 7.55 (d, <i>J</i> = 8.0 Hz, 1H), 7.39-7.43 (m, 2H), 7.24 (m, <i>J</i> = 7.6 Hz, 1H), 6.95 (t, <i>J</i> = 7.6 Hz, 2H), 6.76 (d, <i>J</i> = 7.6 Hz, 1H), 4.74 (m, 1H), 3.87 (br, 4H), 3.63- 3.73 (m, 14H), 3.54 (s, 3H), 3.46-3.48 (m, 2H), 3.37                                                                                                      | C |

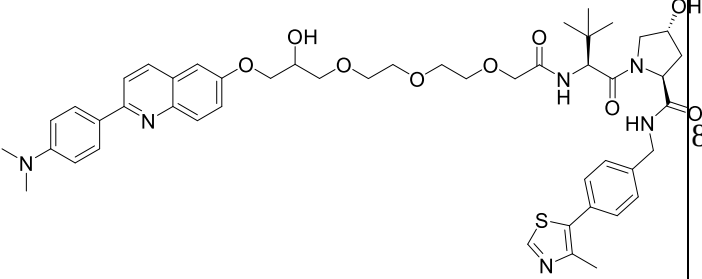
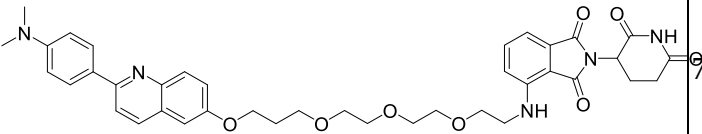
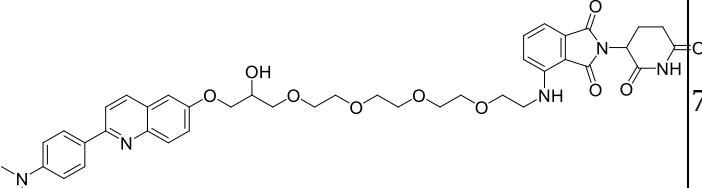
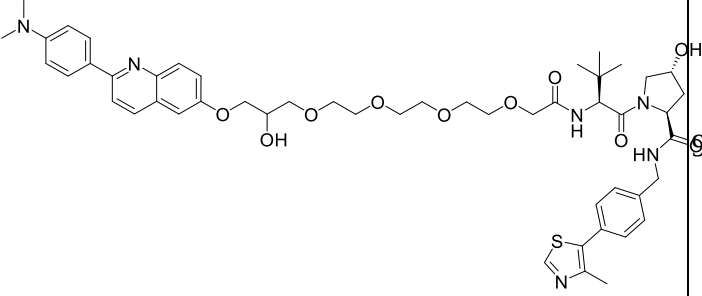
|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                              |   |
|----|-------------------------------------------------------------------------------------|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
|    |                                                                                     |       | (s, 1H), 2.47 ( t, $J$ = 6.8 Hz, 2H), 2.33 (t, $J$ = 6.8 Hz, 2H).                                                                                                                                                                                                                                                                                                                                                                                            |   |
| 26 |    | 729.4 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 8.65 (d, $J$ = 8.0 Hz, 1H), 7.77 (d, $J$ = 8.0 Hz, 1H ), 7.54 (d, $J$ = 8.0 Hz, 1H ), 7.35-7.4 3 (m, 2H), 7.24 (t, $J$ = 8.0 Hz, 1H), 6.95 (t, $J$ = 8.8 Hz, 2H), 6.75 (d, $J$ = 7.6 Hz, 1H), 5.03 (dd, $J$ = 4.2, 12.4 Hz, 1H), 4.58 (br, 4H), 3.70 (br, 4H), 3.60-3.70 (m, 18H), 3.45-3.46 (m, 2H), 2.80-2.85 (m, 1H), 2.66-2.75 (m, 2H), 2.09-2.12 (m, 1H).                                           | C |
| 27 |   | 823.7 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.02-1.05 (m, 9H), 2.07-2.13 (m, 1H), 2.21-2.26 (m, 1H), 2.43-2.47 (m, 3H), 3.05 (s, 6H), 3.76-3.83 (m, 5H), 3.88-3.99 (m, 3H), 4.07-4.12 (m, 2H), 4.30-4.35 (m, 3H), 4.47-4.52 (m, 2H), 4.57-4.61 (m, 1H), 4.71-4.73 (m, 1H), 6.87-6.90 (m, 2H), 7.24-7.29 (m, 1H), 7.35-7.43 (m, 5H), 7.70-7.72 (m, 1H), 7.81-7.83 (m, 1H), 7.91-7.96 (m, 3H), 8.14-8.17 (m, 1H), 8.84 (s, 1H).                         | C |
| 28 |  | 837.7 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.04 (s, 9H), 1.42-1.58 (m, 3H), 1.94-2.01 (m, 1H), 2.17-2.23 (m, 1H), 2.46 (s, 3H), 3.04 (s, 6H), 3.75-3.85 (m, 6H), 3.97-3.98 (m, 2H), 4.08-4.09 (m, 2H), 4.33-4.35 (m, 2H), 4.45 (br, 1H), 4.56-4.60 (m, 1H), 4.70-4.72 (m, 1H), 4.94-4.97 (m, 1H), 6.87-6.90 (m, 2H), 7.30-7.43 (m, 6H), 7.68-7.71 (m, 1H), 7.84-7.86 (m, 1H), 7.95-7.98 (m, 3H), 8.19-8.21 (m, 1H), 8.45-8.47 (m, 1H), 8.86 (s, 1H). | C |

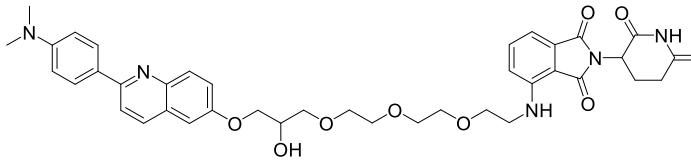
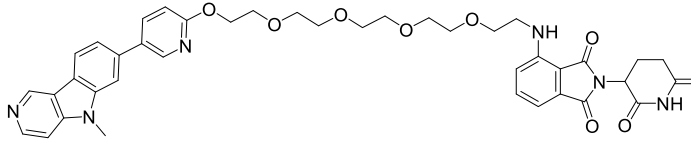
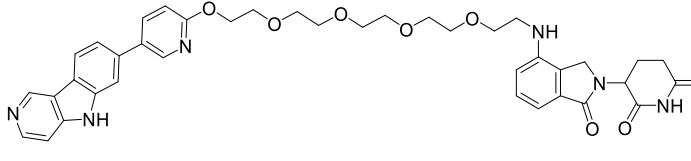
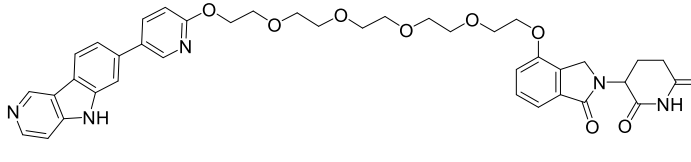
|    |  |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |
|----|--|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
| 29 |  | 867.7 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.02 (s, 9H), 2.07-2.13 (m, 1H), 2.21-2.26 (m, 1H), 2.46 (s, 3H), 3.05 (s, 6H), 3.72-3.77 (m, 9H), 3.87-3.92 (m, 3H), 3.99-4.09 (m, 2H), 4.26-4.58 (m, 2H), 4.33-4.37 (m, 1H), 4.50-4.54 (m, 2H), 4.57-4.61 (m, 1H), 4.70-4.72 (m, 1H), 6.89 (d, <i>J</i> = 8.8 Hz, 2H), 7.26 (d, <i>J</i> = 2.8 Hz, 1H), 7.37-7.45 (m, 5H), 7.66 (d, <i>J</i> = 9.6 Hz, 1H), 7.85 (d, <i>J</i> = 8.4 Hz, 1H), 7.94-7.98 (m, 3H), 8.19 (d, <i>J</i> = 8.8 Hz, 1H), 8.86 (s, 1H). | C |
| 30 |  | 881.4 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.04 (s, 9H), 1.46-1.53 (m, 3H), 1.96-2.04 (m, 1H), 2.19-2.21 (m, 1H), 2.49 (s, 3H), 3.05 (s, 6H), 3.73-3.81 (m, 9H), 3.84-3.87 (m, 1H), 3.95-3.97 (m, 2H), 4.04-4.06 (m, 2H), 4.30-4.33 (m, 2H), 4.44-4.46 (m, 1H), 4.54-4.61 (m, 2H), 4.70 (s, 1H), 4.96-5.00 (m, 1H), 6.89 (m, 2H), 7.29-7.30 (m, 1H), 7.36-7.43 (m, 5H), 7.86 (d, <i>J</i> = 8.8 Hz, 1H), 7.94-7.98 (m, 3H), 8.20 (d, <i>J</i> = 8.8 Hz, 1H), 8.86 (s, 1H).                                  | C |
| 31 |  | 911.4 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 1.04 (s, 9H), 2.07-2.15 (m, 1H), 2.22-2.26 (m, 1H), 2.47 (s, 3H), 3.06 (s, 6H), 3.61-3.75 (s, 12H), 3.82-3.83 (m, 1H), 3.89-3.93 (m, 2H), 4.01-4.07 (m, 2H), 4.28-4.40 (m, 3H), 4.49-4.69 (m, 5H), 6.87-6.97 (m, 2H), 7.27-7.42 (m, 6H), 7.62-7.67 (br, 1H), 7.83-7.98 (m, 4H), 8.17-8.23 (m, 1H), 8.88 (s, 1H).                                                                                                                                                | C |
| 32 |  | 925.4 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 1.06 (s, 9H), 1.50-1.58 (m, 3H), 1.94-2.03 (m, 1H), 2.17-2.25 (m, 1H), 2.48 (s, 3H), 3.06 (s, 6H), 3.70-3.77 (m, 12H), 3.85-3.89 (s, 1H), 3.90-4.05 (m, 4H), 4.29-4.35 (m, 2H), 4.43-4.49 (m, 1H), 4.56-4.61                                                                                                                                                                                                                                                    | C |

|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |   |
|----|-------------------------------------------------------------------------------------|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
|    |                                                                                     |       | (m, 1H), 4.67-4.71 (m, 1H), 4.99-5.02 (m, 2H), 6.88-6.91 (m, 2H), 7.30-7.41 (m, 5H), 7.63-7.66 (m, 1H), 7.87-7.99 (m, 4H), 8.19-8.23 (m, 1H), 8.50-8.52 (m, 1H), 8.87 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                   |   |
| 33 |   | 807.4 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 1.05 (s, 9H), 1.89-2.03 (m, 4H), 2.10-2.14 (m, 1H), 2.22-2.26 (m, 1H), 2.46 (s, 3H), 3.05 (s, 6H), 3.67-3.70 (m, 2H), 3.81-3.91 (m, 2H), 3.98-4.09 (m, 2H), 4.17-4.20 (m, 2H), 4.34-4.38 (m, 1H), 4.53-4.62 (m, 3H), 7.71-7.73 (m, 1H), 6.88-6.91 (m, 2H), 7.24-7.28 (m, 1H), 7.34-7.47 (m, 5H), 7.58-7.60 (m, 1H), 7.82-7.84 (m, 1H), 7.91-7.97 (m, 3H), 8.15-8.17 (m, 1H), 8.83 (s, 1H).                                                                                                                   | C |
| 34 |  | 821.4 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 1.04 (s, 9H), 1.49-1.60 (m, 3H), 1.89-1.95 (m, 2H), 1.97-2.03 (m, 3H), 2.19-2.24 (m, 1H), 2.48 (s, 3H), 3.05 (s, 6H), 3.69 (t, <i>J</i> = 6.0 Hz, 2H), 3.75-3.79 (m, 1H), 3.85-3.88 (m, 1H), 3.99-4.09 (m, 2H), 4.19-4.22 (m, 2H), 4.46 (br, 1H), 4.56-4.62 (m, 1H), 4.70-4.73 (m, 1H), 4.98-5.05 (m, 1H), 6.88-6.91 (m, 2H), 7.27-7.29 (m, 1H), 7.38-7.44 (m, 5H), 7.57 (d, <i>J</i> = 9.6 Hz, 1H), 7.80-7.87 (m, 1H), 7.94-7.98 (m, 3H), 8.76-8.22 (m, 1H), 8.52 (d, <i>J</i> = 7.6 Hz, 1H), 8.86 (s, 1H). | C |
| 35 |  | 851.4 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 1.03 (s, 9H), 1.91-1.92 (m, 2H), 2.05-2.26 (m, 4H), 2.45 (s, 3H), 3.04 (s, 6H), 3.62-3.68 (m, 6H), 3.79-4.00 (m, 4H), 4.15-4.25 (m, 2H), 4.33-4.36 (m, 1H), 4.50-4.61 (m, 3H), 4.69-4.71 (m, 1H), 6.88 (d, <i>J</i> = 8.0 Hz, 2H), 7.22-7.26 (m, 1H), 7.31-7.43 (m, 4H), 7.54 (d, <i>J</i> = 8.4 Hz, 1H), 7.81-7.96 (m, 4H),                                                                                                                                                                                 | C |

|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |
|----|-------------------------------------------------------------------------------------|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
|    |                                                                                     |       | 8.16 (d, $J$ = 8.4 Hz, 1H),<br>8.84, 8.86 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |
| 36 |    | 865.6 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): $\delta$ 1.04 (s, 9H), 1.46-1.58 (m, 3H), 1.92-2.00 (m, 3H), 2.12-2.21 (m, 3H), 2.47 (s, 3H), 3.04 (s, 6H), 3.62-3.97 (m, 10H), 4.23 (t, $J$ = 5.2 Hz, 2H), 4.35-4.45 (m, 1H), 4.57-4.70 (m, 2H), 4.98-5.01 (m, 1H), 6.88 (d, $J$ = 8.4 Hz, 2H), 7.27-7.56 (m, 7H), 7.79-8.02 (m, 4H), 8.17-8.23 (m, 1H), 8.52 (d, $J$ = 6.8 Hz, 1H), 8.87 (s, 1H).                                                                                                                                                                                                                          | C |
| 37 |  | 821.4 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): $\delta$ 1.03, 1.05 (dos singletes, 9H), 1.64-1.72 (m, 2H), 1.74-1.80 (m, 2H), 1.88-1.95 (m, 2H), 2.07-2.14 (m, 1H), 2.22-2.27 (m, 1H), 2.43, 2.46 (dos singletes, 3H), 3.04 (s, 6H), 3.63 (t, $J$ = 6.0 Hz, 2H), 3.80-3.83 (m, 1H), 3.88-3.91 (m, 1H), 3.96-4.05 (m, 2H), 4.13 (t, $J$ = 6.4 Hz, 2H), 4.32-4.34 (m, 1H), 4.48-4.55 (m, 2H), 4.58-4.63 (m, 1H), 4.69-4.74 (m, 1H), 6.88 (d, $J$ = 8.8 Hz, 2H), 7.20 (s, 1H), 7.33-7.46 (m, 5H), 7.57 (d, $J$ = 9.6 Hz, 1H), 7.81 (d, $J$ = 6.0Hz, 1H), 7.93 (t, $J$ = 10.0 Hz, 3H), 8.14 (d, $J$ = 8.8 Hz, 1H), 8.81 (s, 1H). | C |
| 38 |  | 835.4 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): $\delta$ 1.04 (s, 9H), 1.44-1.58 (m, 3H), 1.66-1.81 (m, 4H), 1.89-2.02 (m, 3H), 2.14-2.31 (m, 1H), 2.46 (s, 3H), 3.05 (s, 6H), 3.63 (t, $J$ = 6.4 Hz, 2H), 3.74-3.78 (m, 1H), 3.85-3.88 (m, 1H), 3.96-4.06 (m, 2H), 4.14-4.19 (m, 2H), 4.37-4.46 (m, 1H), 4.56-4.62 (m, 1H), 4.67-4.77 (m, 1H), 4.94-5.04 (m, 1H), 6.89 (d, $J$ = 9.2 Hz, 2H), 7.26 (t, $J$ = 3.2 Hz, 1H), 7.35-7.43 (m, 5H), 7.56 (d, $J$ = 9.6 Hz, 1H), 7.81-7.88 (m, 1H), 8.00-7.91 (m, 3H), 8.18 (d, $J$ = 8.4 Hz, 1H), 8.49 (d, $J$ = 7.2 Hz, 1H), 8.86 (s, 1H).                                         | C |

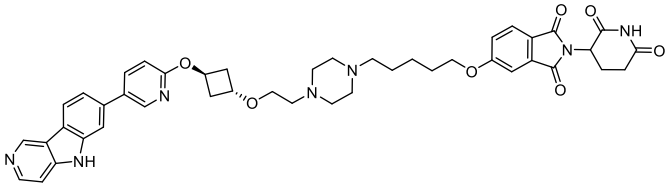
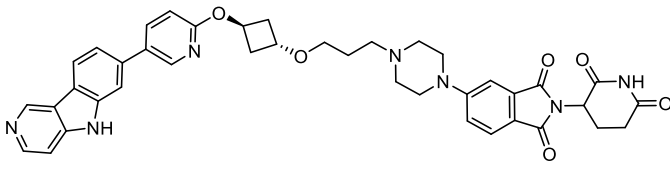
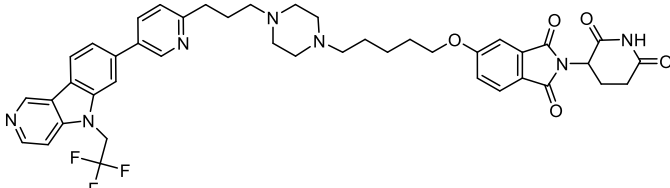
|    |  |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |   |
|----|--|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
| 39 |  | 939.4 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.04 (s, 9H), 1.48-1.57 (m, 3H), 1.95-2.22 (m, 5H), 2.47 (s, 3H), 3.06 (s, 6H), 3.60-3.66 (m, 12H), 3.70-3.86 (m, 4H), 3.97-4.06 (m, 2H), 4.24 (t, <i>J</i> = 6.0 Hz, 2H), 4.44 (br, 1H), 4.58 (t, <i>J</i> = 8.4 Hz, 1H), 4.68-4.70 (m, 1H), 4.99-5.02 (m, 1H), 6.89 (d, <i>J</i> = 8.4 Hz, 2H), 7.27 (s, 1H), 7.37-7.43 (m, 5H), 7.61-7.63 (m, 1H), 7.84 (d, <i>J</i> = 8.4 Hz, 1H), 7.95-7.97 (m, 3H), 7.81-7.82 (m, 1H), 8.86(s, 1H). | C |
| 40 |  | 754.4 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.92-2.00 (m, 2H), 2.55-2.74 (m, 4H), 2.93 (s, 6H), 3.28-3.37 (m, 4H), 3.46-3.53 (m, 12H), 3.60 (t, <i>J</i> = 6.2 Hz, 2H), 4.11 (t, <i>J</i> = 6.2 Hz, 2H), 4.89-4.93 (m, 1H), 6.41-6.44 (m, 1H), 6.76 (d, <i>J</i> = 8.8 Hz, 2H), 6.89 (t, <i>J</i> = 7.6 Hz, 2H), 7.13 (d, <i>J</i> = 2.4 Hz, 1H), 7.23-7.26 (m, 1H), 7.36-7.40 (m, 1H), 7.69 (d, <i>J</i> = 8.8 Hz, 1H), 7.80-7.84 (m, 3H), 8.05 (d, <i>J</i> = 8.8 Hz, 1H).          | C |
| 41 |  | 699.4 | <sup>1</sup> H NMR (400 MHz, MeOD): δ 8.46 (d, <i>J</i> = 8.0 Hz, 1H), 7.64 (d, <i>J</i> = 8.0 Hz, 1H), 7.45 (d, <i>J</i> = 8.0 Hz, 1H), 7.27 (t, <i>J</i> = 7.6 Hz, 1H), 7.06-7.14 (m, 2H), 6.57-6.71 (m, 3H), 4.89-4.96 (m, 1H), 4.18 (s, 2H), 3.84 (s, 2H), 3.46-3.70 (m, 16H), 3.30 (s, 2H), 2.58-2.76 (m, 3H), 1.99-2.07 (m, 3H).                                                                                                                                                       | C |
| 42 |  | 743.7 | <sup>1</sup> H NMR (400MHz, MeOD): δ 8.65 (d, <i>J</i> = 8.0 Hz, 1H), 7.77 (d, <i>J</i> = 8.0 Hz, 1H), 7.55 (d, <i>J</i> = 8.0 Hz, 1H), 7.31-7.40 (m, 2H), 7.21-7.28 (m, 1H), 6.84-7.90 (m, 2H), 6.76 (d, <i>J</i> = 8,0 Hz, 1H), 5.00-5.04 (m, 1H), 4.30 (s, 2H), 3.85-3.95 (m, 4H), 3.63-3.70 (m, 18H), 3.38 (s, 2H), 2.61-2.90 (m, 3H), 2.02-2.21 (m, 1H).                                                                                                                                | C |

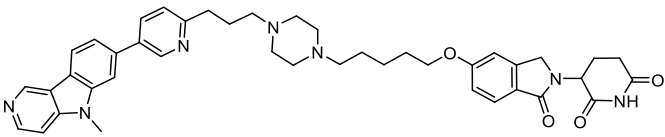
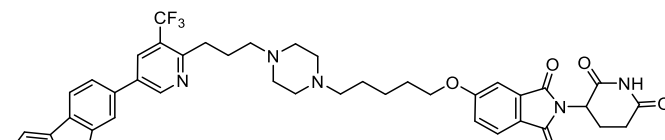
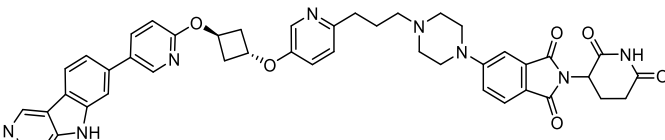
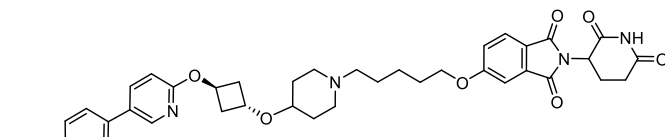
|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |   |
|----|-------------------------------------------------------------------------------------|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
| 43 |    | 897.4 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.04 (s, 9H), 2.05-2.13 (m, 1H), 2.21-2.23 (m, 1H), 2.46 (s, 3H), 3.05 (s, 6H), 3.65-3.74 (m, 10H), 3.79-3.90 (m, 2H), 3.98-4.07 (m, 2H), 4.13-4.22 (m, 3H), 4.33-4.37 (m, 1H), 4.50-4.62 (m, 3H), 4.70 (s, 1H), 6.89 (d, <i>J</i> = 8.8 Hz, 2H), 7.25-7.26 (m, 1H), 7.38-7.44 (m, 5H), 7.83 (d, <i>J</i> = 8.8 Hz, 1H), 7.94-7.97 (m, 3H), 8.17 (d, <i>J</i> = 8.8 Hz, 1H), 8.85 (s, 1H).                                         | C |
| 44 |   | 710.3 | <sup>1</sup> HNMR (400 MHz, CDCl <sub>3</sub> ): δ 2.07-2.13 (m, 4H), 2.68-2.88 (m, 4H), 3.04 (s, 6H), 3.33-3.45 (m, 2H), 3.64-3.69 (m, 11H), 4.16-4.18 (m, 2H), 4.86-4.90 (m, 1H), 6.42-6.44 (m, 1H), 6.81-6.85 (m, 3H), 7.06-7.07 (m, 2H), 7.32 (d, <i>J</i> = 8.8 Hz, 1H), 7.41-7.45 (m, 1H), 7.74-7.77 (m, 1H), 7.98-8.07 (m, 5H).                                                                                                                                                | C |
| 45 |  | 770.3 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 2.07-2.11 (m, 1H), 2.62-2.87 (m, 4H), 3.04 (s, 6H), 3.40-3.43 (m, 2H), 3.65-3.78 (m, 16H), 4.13 (d, <i>J</i> = 5.2 Hz, 2H), 4.24 (t, <i>J</i> = 4.2 Hz, 1H), 4.87-4.91 (m, 1H), 6.45-6.47 (m, 1H), 6.81-6.87 (m, 3H), 7.06, 7.07 (dos singletes, 2H), 7.33-7.36 (m, 1H), 7.44 (t, <i>J</i> = 7.8 Hz, 1H), 7.76 (d, <i>J</i> = 8.8 Hz, 1H), 8.01-8.10 (m, 4H), 8.56 (br. s, 1H).                                                   | C |
| 46 |  | 941.4 | <sup>1</sup> HNMR (400 MHz, CD <sub>3</sub> OD): δ 1.02, 1.04 (dos singletes, 9H), 2.05-2.12 (m, 1H), 2.21-2.27 (m, 1H), 2.46, 2.47 (dos singletes, 3H), 3.07 (s, 6H), 3.63-3.70 (m, 14H), 3.79-3.90 (m, 2H), 3.98-4.07 (m, 2H), 4.13-4.24 (m, 3H), 4.33-4.37 (m, 1H), 4.50-4.61 (m, 3H), 4.69-4.71 (m, 1H), 6.89 (d, <i>J</i> = 8.8 Hz, 2H), 7.33-7.48 (m, 6H), 7.90 (d, <i>J</i> = 8.8 Hz, 1H), 7.97-7.99 (m, 3H), 8.17 (d, <i>J</i> = 8.8 Hz, 1H), 8.87, 8.88 (dos singletes, 1H). | C |

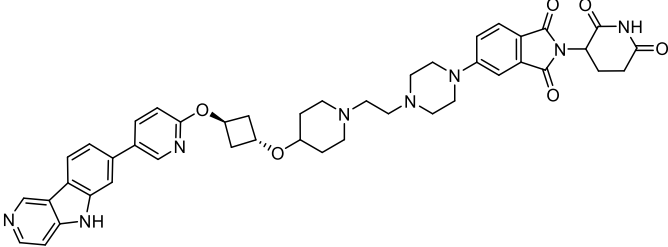
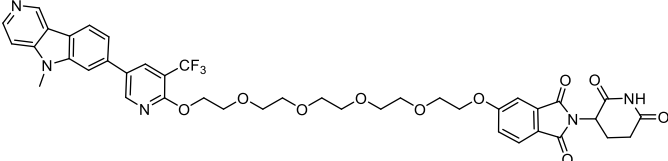
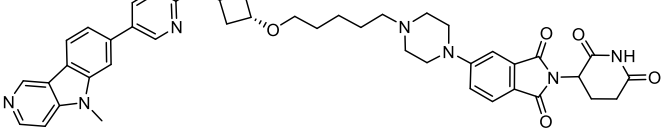
|    |                                                                                     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |   |
|----|-------------------------------------------------------------------------------------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
| 47 |    | 726.3 | <sup>1</sup> H NMR (400 Hz, CDCl <sub>3</sub> ): δ 2.01-2.24 (m, 2H), 2.68-2.88 (m, 3H), 3.04 (s, 6H), 3.24 (s, 1H), 3.43 (s, 2H), 3.69 (s, 10H), 4.15-4.24 (m, 3H), 4.83-4.96 (m, 1H), 5.27-5.42 (m, 1H), 6.48 (s, 1H), 6.77-6.83 (m, 3H), 7.07 (s, 2H), 7.34-7.44 (m, 2H), 7.73-7.83 (m, 1H), 7.98-8.05 (m, 4H), 8.27 (s, 1H).                                                                                                                                                                                                                                                                                                          | C |
| 48 |   | 751.2 | <sup>1</sup> H NMR (400 MHz, MeOD): δ 9.24 (s, 1H), 8.50 (d, <i>J</i> = 2.0 Hz 1H), 8.45 (d, <i>J</i> = 5.6 Hz, 2H), 8.26 (d, <i>J</i> = 8.4 Hz, 1H), 8.06–8.09 (m, 1H), 7.80 (s, 1H), 7.57 (t, <i>J</i> = 8.0 Hz, 2H), 7.44 (t, <i>J</i> = 8.4 Hz, 1H), 6.98 (d, <i>J</i> = 8.4 Hz, 1H), 6.92–6.94 (m, 2H), 4.95–5.09 (m, 1H), 4.49–4.53 (m, 2H), 3.96 (s, 3H), 3.88 (d, <i>J</i> = 4.8 Hz, 2H), 3.63–3.70 (m, 14H), 3.41 (t, <i>J</i> = 6.4 Hz, 2H), 2.64–2.82 (m, 3H).                                                                                                                                                                 | A |
| 49 |  | 723.3 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.36 (s, 1H), 8.39-8.45 (m, 3H), 8.30 (d, <i>J</i> = 8.0 Hz, 1H), 8.01 (dd, <i>J</i> = 2.4, 6.4 Hz, 1H), 7.78 (s, 1H), 7.70 (d, <i>J</i> = 6.0 Hz, 1H), 7.59 (d, <i>J</i> = 8.4 Hz, 1H), 7.26 (t, <i>J</i> = 7.6 Hz, 1H), 7.03 (d, <i>J</i> = 7.6 Hz, 1H), 6.90 (d, <i>J</i> = 8.8 Hz, 1H), 6.80 (d, <i>J</i> = 8.0 Hz, 1H), 5.12 (dd, <i>J</i> = 5.2, 13.6 Hz, 1H), 4.47 (t, <i>J</i> = 4.4 Hz, 2H), 4.27 (d, <i>J</i> = 2.4 Hz, 2H), 3.85 (d, <i>J</i> = 4.4 Hz, 2H), 3.62-3.68 (m, 14H), 3.36 (t, <i>J</i> = 5.6 Hz, 2H), 2.75-2.95 (m, 2H), 2.35-2.47 (m, 1H), 2.10-2.21 (m, 1H). | A |
| 50 |  | 724.3 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 9.29 (s, 1H), 8.52 (s, 1H), 8.36 (s, 1H), 8.13 (d, <i>J</i> = 8.0 Hz, 1H), 7.81 (d, <i>J</i> = 8.0 Hz, 1H), 7.53 (s, 1H), 7.34-7.43 (m, 4H), 6.99 (d, <i>J</i> = 8.4 Hz, 1H), 6.82 (d, <i>J</i> = 8.8 Hz, 1H), 5.16-5.21 (m, 1H), 4.52 (s, 2H), 4.39-4.43 (m, 1H), 4.27-4.31                                                                                                                                                                                                                                                                                                          | A |

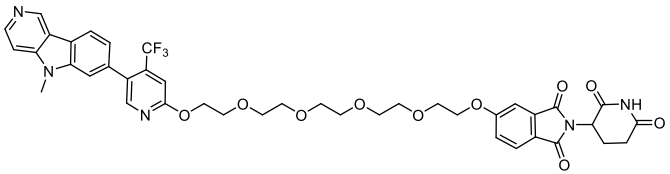
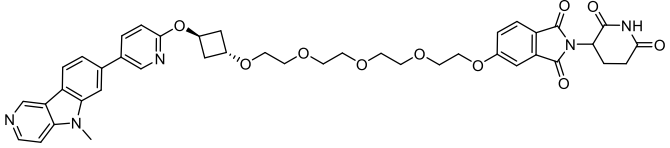
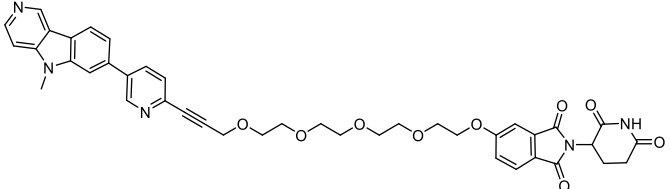
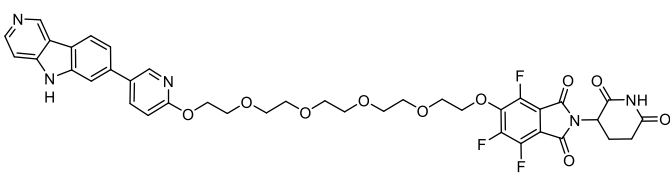


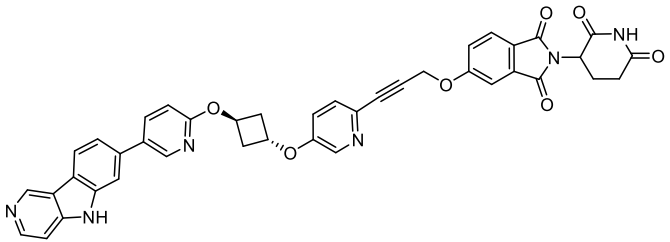
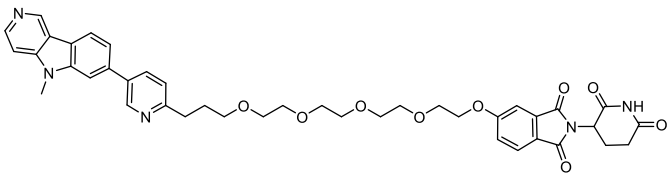
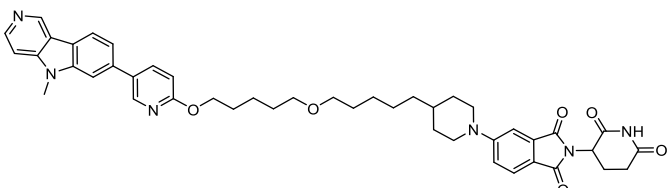
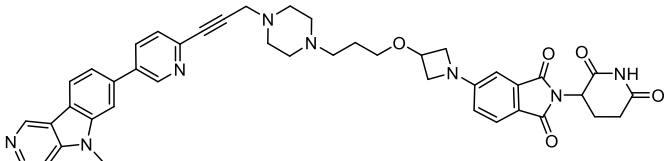
|    |  |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|----|--|---|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 54 |  | C | 714.3 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.31 (s, 1H), 8.83 (s, 1H), 8.42 (d, <i>J</i> = 6.1 Hz, 2H), 8.34 (d, <i>J</i> = 8.3 Hz, 1H), 8.14 (d, <i>J</i> = 8.0 Hz, 1H), 7.84 (s, 1H), 7.78 (d, <i>J</i> = 8.5 Hz, 1H), 7.61 (dd, <i>J</i> = 16.5, 6.4 Hz, 2H), 7.47 (d, <i>J</i> = 8.3 Hz, 1H), 7.36 (s, 1H), 7.28 (d, <i>J</i> = 8.2 Hz, 1H), 5.06 – 5.13 (m, 1H), 4.14 (s, 2H), 2.83 (m, 18H), 2.04 (s, 3H), 1.87 (s, 2H), 1.69 (s, 2H), 1.55 (s, 2H).                                                                                            |
| 55 |  | C | 763.3 | <sup>1</sup> H NMR (400 MHz, MeOD): δ 9.62 (s, 1H), 9.03 (s, 1H), 8.58 (d, <i>J</i> = 6.8 Hz, 1H), 8.52 (d, <i>J</i> = 8.0 Hz, 1H), 8.31-8.40 (m, 1H), 8.08 (s, 1H), 7.87-7.99 (m, 2H), 7.78-7.87 (m, 3H), 7.68-7.72 (m, 1H), 7.26-7.30 (m, 2H), 7.10-7.14 (m, 1H), 5.08-5.12 (m, 1H), 4.17 (t, <i>J</i> = 6.0 Hz, 2H), 3.81-3.92 (m, 4H), 3.50-3.60 (m, 4H), 3.30-3.40 (m, 2H), 3.10-3.18 (m, 2H), 2.71-2.86 (m, 5H), 2.30-2.33 (m, 2H), 2.10-2.16 (m, 3H).                                                                                                   |
| 56 |  | C | 786.3 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ) δ 9.33 (s, 1H), 8.89 (s, 1H), 8.53 (s, 1H), 8.42 (s, 1H), 8.18 (d, <i>J</i> = 8.2 Hz, 1H), 7.87 (d, <i>J</i> = 6.2 Hz, 1H), 7.77 (d, <i>J</i> = 8.2 Hz, 1H), 7.62 (s, 1H), 7.49 (d, <i>J</i> = 7.7 Hz, 1H), 7.42 (s, 1H), 7.29 (d, <i>J</i> = 11.5 Hz, 1H), 7.17 (d, <i>J</i> = 6.5 Hz, 1H), 6.82 (d, <i>J</i> = 8.2 Hz, 1H), 5.34 (s, 2H), 5.00 – 4.87 (m, 1H), 4.07 (s, 2H), 3.75 (s, 1H), 3.57 (s, 1H), 3.04 – 2.49 (m, 10H), 2.20 (m, 4H), 2.01 (s, 4H), 1.85 (s, 3H), 1.75 – 1.55 (m, 3H), 1.52 (s, 2H). |
| 57 |  | C | 728.3 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.30 (s, 1H), 8.42-8.60 (m, 2H), 8.19 (d, <i>J</i> = 8.0 Hz, 1H), 7.60-7.65 (m, 2H), 7.52 (s, 1H), 7.31 (d, <i>J</i> = 8.0 Hz, 1H), 7.19 (s, 1H), 7.12-7.14 (m, 1H), 5.07-5.10 (m, 1H), 4.12 (t, <i>J</i> = 4.0 Hz, 2H), 3.66-3.86 (m, 18H), 3.37 (s, 2H), 3.15-3.20 (m, 3H), 2.71-2.76 (m, 3H), 2.09-2.22 (m, 5H).                                                                                                                                                                                        |
| 58 |  | C | 758.3 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.25 (s, 1H), 8.79 (s, 1H), 8.39 (d, <i>J</i> = 6.0 Hz, 1H), 8.30 (d, <i>J</i> = 8.0 Hz, 1H), 8.12 (d, <i>J</i> = 8.0 Hz, 1H), 7.79                                                                                                                                                                                                                                                                                                                                                                        |

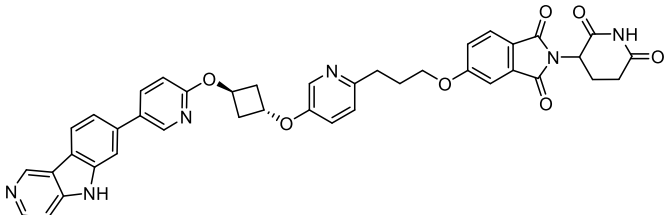
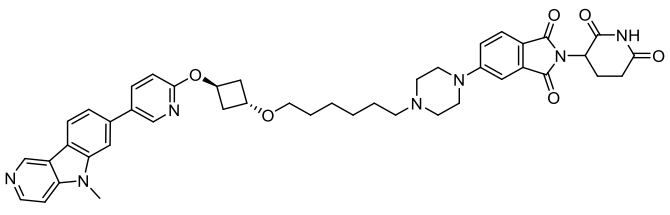
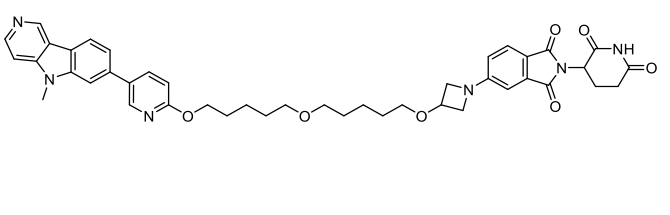
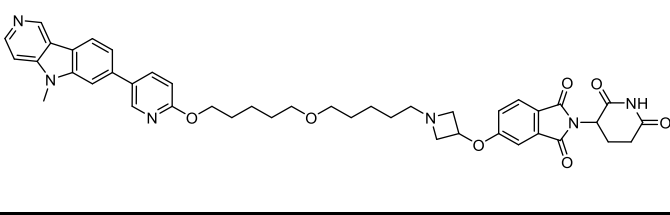
|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|----|-------------------------------------------------------------------------------------|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                     |   |       | (s, 1H), 7.76 (d, $J$ = 8.4 Hz, 1H), 7.59 (d, $J$ = 8.0 Hz, 1H), 7.52 (d, $J$ = 5.2 Hz, 1H), 7.44 (d, $J$ = 8.0 Hz, 1H), 7.35 (d, $J$ = 6.0 Hz, 1H), 5.07-5.09 (m, 1H), 4.13 (t, $J$ = 6.4 Hz, 2H), 3.59 (t, $J$ = 5.2 Hz, 2H), 3.47 (t, $J$ = 6.0 Hz, 2H), 2.47-2.88 (m, 16H), 1.98-2.1 (m, 4H), 1.80-1.84 (m, 2H), 1.55-1.57 (m, 5H).                                                                                                                                                                                                                                                                                                                                                             |
| 59 |   | C | 786.3 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ 11.79 (s, 1H), 11.11 (s, 1H), 9.35 (s, 1H), 8.55 (s, 1H), 8.42 (d, $J$ = 5.4 Hz, 1H), 8.29 (d, $J$ = 8.2 Hz, 1H), 8.17 (s, 1H), 8.11 (d, $J$ = 8.6 Hz, 1H), 7.82 (d, $J$ = 8.6 Hz, 1H), 7.76 (s, 1H), 7.55 (d, $J$ = 8.2 Hz, 1H), 7.48 (d, $J$ = 5.6 Hz, 1H), 7.42 (s, 1H), 7.34 (d, $J$ = 8.0 Hz, 1H), 6.93 (d, $J$ = 8.6 Hz, 1H), 5.31 (s, 1H), 5.11 (dd, $J$ = 12.9, 5.2 Hz, 1H), 4.17 (d, $J$ = 6.7 Hz, 3H), 3.42 (d, $J$ = 5.4 Hz, 2H), 2.96 – 2.78 (m, 2H), 2.60 (dd, $J$ = 34.5, 18.5 Hz, 2H), 2.37 (dd, $J$ = 44.1, 5.8 Hz, 13H), 2.01 (d, $J$ = 14.9 Hz, 2H), 1.76 (s, 2H), 1.41 (dd, $J$ = 43.8, 29.4 Hz, 4H), 1.23 (s, 2H). |
| 60 |  | C | 714.3 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 11.07 (s, 1H), 9.76 (s, 1H), 8.67 (d, $J$ = 6.0 Hz, 1H), 8.60 (s, 1H), 8.52 (d, $J$ = 8.4 Hz, 1H), 8.16 (d, $J$ = 8.4 Hz, 1H), 8.80-8.02 (m, 2H), 7.77 (t, $J$ = 8.4 Hz, 2H), 7.50 (s, 1H), 7.37 (d, $J$ = 8.0 Hz, 1H), 6.96 (d, $J$ = 8.8 Hz, 1H), 5.36 (m, 1H), 5.07-5.11 (m, 1H), 4.24 (br, 3H), 3.62 (br, 9H), 3.55 (s, 3H), 3.17-3.25 (m, 6H), 2.86-2.93 (m, 1H), 2.38-2.62 (m, 4H), 1.97-2.04 (m, 1H).                                                                                                                                                                                                                          |
| 61 |  | C | 796.3 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD) δ 9.35 (s, 1H), 8.89 (s, 1H), 8.55 (d, $J$ = 5.8 Hz, 1H), 8.40 (d, $J$ = 8.0 Hz, 1H), 8.17 – 8.22 (m, 1H), 8.05 (s, 1H), 7.81 (d, $J$ = 8.3 Hz, 1H), 7.74 (d, $J$ = 5.6 Hz, 1H), 7.51 (d, $J$ = 8.2 Hz, 1H), 7.40 (s, 1H), 7.33 (s, 1H), 5.40 (d, $J$ = 9.1 Hz, 2H), 5.08 – 5.16 (m, 1H), 4.95 (s, 4H), 4.59 (s, 2H), 4.18 (t, $J$ = 6.2 Hz, 1H), 2.91 – 3.00 (m, 2H), 2.58 – 2.91 (m, 9H), 2.12 – 2.18 (m, 1H), 2.06 (s, 2H), 1.89 (s,                                                                                                                                                                                                            |

|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|----|-------------------------------------------------------------------------------------|---|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                     |   |       | 2H), 1.69 (s, 2H), 1.57 (s, 2H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 62 |    | C | 714.3 | <sup>1</sup> H NMR(400 MHz, MeOD): $\delta$ 9.27 (s, 1H), 8.86 (d, $J$ =2.0 Hz, 1H), 8.46 (d, $J$ =6.0 Hz, 1H), 8.33 (d, $J$ =8.0 Hz, 1H), 8.16 (d, $J$ =2.4 Hz, 1H), 7.90 (s, 1H), 7.59-7.70 (m, 3H), 7.47 (d, $J$ =6.0 Hz, 1H), 7.03-7.09 (m, 2H), 5.06-5.12 (m, 1H), 4.42 (d, $J$ =5.6 Hz, 2H), 4.07 (t, $J$ =6.4 Hz, 2H), 3.99 (s, 3H), 2.89-2.96 (m, 3H), 2.51-2.75 (m, 13H), 2.12-2.24 (m, 1H), 2.01-2.03 (m, 3H), 1.82-1.84 (m, 2H), 1.52-1.63 (m, 6H).                                                       |
| 63 |  | C | 796.2 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): $\delta$ 9.25 (s, 1H), 8.45 (s, 1H), 8.23(d, $J$ = 7.6 Hz, 1H), 7.76 (d, $J$ = 8.4 Hz, 1H), 7.66 (s, 1H), 7.59 (d, $J$ = 8.0 Hz, 1H), 7.39 (d, $J$ = 8.4 Hz, 1H), 7.35 (s, 2H), 7.26-7.28 (m, 1H), 6.06 (s, 1H), 5.72 (s, 1H), 5.06–5.08 (m, 1H), 4.11–4.15 (m, 2H), 3.90–3.94 (m, 4H), 3.70–3.74 (m, 2H), 3.03–3.06 (m, 2H), 2.82–2.88 (m, 4H), 2.71–2.75 (m, 6H), 2.51–2.55 (m, 3H), 2.05–2.25 (m, 2H), 1.82–1.86 (m, 2H), 1.61–1.63 (m, 2H), 1.51–1.52 (m, 2H). |
| 64 |  | C | 791.2 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD) $\delta$ 9.42 (s, 1H), 8.53 (d, $J$ = 2.3 Hz, 1H), 8.50 (d, $J$ = 6.1 Hz, 1H), 8.38 (d, $J$ = 8.1 Hz, 1H), 8.13 (d, $J$ = 8.0 Hz, 2H), 7.87 (s, 1H), 7.71–7.78 (m, 2H), 7.68 (d, $J$ = 8.3 Hz, 1H), 7.42 (s, 1H), 7.33 (s, 2H), 7.29 (d, $J$ = 8.6 Hz, 1H), 6.99 (d, $J$ = 8.6 Hz, 1H), 5.51 (s, 2H), 5.06–5.14 (m, 2H), 3.55 (s, 4H), 2.58–3.03 (m, 15H), 2.04 (m, 3H).                                                                                            |
| 65 |  | C | 757.5 | <sup>1</sup> H NMR: (400 MHz, DMSO-d <sub>6</sub> ) $\delta$ : 11.80 (s, 1H), 11.11 (s, 1H), 9.35 (s, 1H), 8.55 (d, $J$ =2.4 Hz, 1H), 8.42 (d, $J$ =5.6 Hz, 1H), 8.29 (d, $J$ =8.4 Hz, 1H), 8.18 (s, 3H), 8.11 (dd, $J$ =2.4, 8.8 Hz, 1H), 7.83 (d, $J$ =8.4 Hz, 1H), 7.76 (s, 1H), 7.55 (d, $J$ =8.4 Hz, 1H), 7.48 (d, $J$ =5.6 Hz, 1H), 7.42 (d, $J$ =2.0 Hz, 1H), 7.35 (dd, $J$ =2.0, 8.4 Hz, 1H), 6.92 (d, $J$ =8.4 Hz, 1H), 5.30 (d, $J$ =3.6                                                                   |

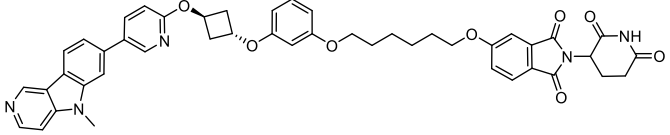
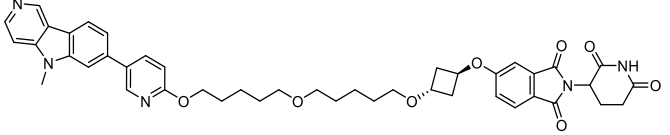
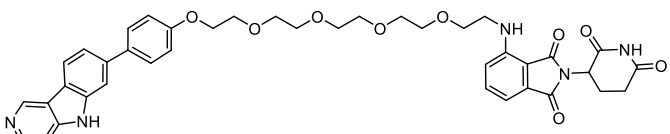
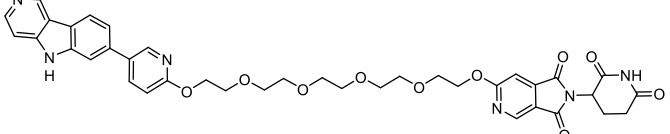
|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|----|-------------------------------------------------------------------------------------|---|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                     |   |       | Hz, 1H), 5.11 (dd, $J$ =5.6, 13.2 Hz, 1H), 4.35 (t, $J$ =6.4 Hz, 1H), 4.17 (t, $J$ =6.4 Hz, 2H), 2.93 - 2.84 (m, 2H), 2.77 (s, 2H), 2.63 - 2.54 (m, 3H), 2.37 (d, $J$ =6.0 Hz, 4H), 2.22 - 1.98 (m, 4H), 1.87 - 1.74 (m, 4H), 1.53 - 1.38 (m, 6H).                                                                                                                                                                                                                                                                                 |
| 66 |    | C | 783.6 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 13.21 (s, 1H), 11.08 (s, 2H), 9.76 (s, 1H), 8.67 (d, $J$ = 6.6 Hz, 1H), 8.61 (s, 1H), 8.52 (d, $J$ = 8.3 Hz, 1H), 8.17 (d, $J$ = 8.3 Hz, 1H), 8.02 (d, $J$ = 7.1 Hz, 2H), 7.82 – 7.72 (m, 3H), 7.46 (s, 2H), 7.35 (s, 2H), 6.96 (d, $J$ = 8.5 Hz, 1H), 5.34 (s, 1H), 5.08 (d, $J$ = 7.7 Hz, 2H), 4.40 (s, 2H), 3.23 (s, 4H), 3.15 (s, 4H), 3.02 (s, 4H), 2.95 – 2.83 (m, 4H), 2.59 (d, $J$ = 15.7 Hz, 4H), 2.44 (s, 2H), 2.01 (s, 5H), 1.77 (d, $J$ = 14.7 Hz, 2H).  |
| 67 |  | A | 820.5 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.25 (s, 1H), 8.79 (s, 1H), 8.37–8.39 (d, $J$ = 8.0 Hz, 1H), 8.28–8.30 (d, $J$ = 8.0 Hz, 2H), 7.89 (s, 1H), 7.63–7.65 (d, $J$ = 8.0 Hz, 1H), 7.54–7.56 (m, 2H), 7.26 (s, 1H), 7.18–7.20 (m, 1H), 5.02–5.05 (m, 1H), 4.62–4.64 (m, 2H), 4.17–4.19 (m, 2H), 3.95 (s, 3H), 3.88–3.90 (m, 2H), 3.82–3.84 (m, 2H), 3.61–3.71 (m, 13H), 2.55–2.81 (m, 3H), 2.95–2.99 (m, 1H).                                                                                                        |
| 68 |  | C | 756.6 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 11.12 (s, 1H), 9.37 (s, 1H), 8.64 (s, 1H), 8.50 (d, $J$ = 4.0 Hz, 1H), 8.33 (d, $J$ = 12.0 Hz, 1H), 8.00 (s, 1H), 7.68–7.60 (m, 3H), 7.34 (d, $J$ = 4.0 Hz, 1H), 7.25 (dd, $J$ = 8.0 Hz, 4.0 Hz, 1H), 6.94 (d, $J$ = 8.0 Hz, 1H), 5.32 (t, $J$ = 4.0 Hz, 1H), 5.07 (dd, $J$ = 12.0 Hz, 8.0 Hz, 1H), 4.20–4.17 (m, 1H), 3.96 (s, 3H), 4.46 (s, 6H), 2.88–2.84 (m, 1H), 2.59–2.54 (m, 7H), 2.43–2.32 (m, 6H), 2.02–1.98 (m, 1H), 1.57–1.49 (m, 4H), 1.38–1.34 (m, 2H). |

|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|----|-------------------------------------------------------------------------------------|---|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 69 |    | A | 820.5 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.21 (s, 1H), 8.79 (s, 1H), 8.38 (d, <i>J</i> = 8.0 Hz, 2H), 7.62(d, <i>J</i> = 8.0 Hz, 1H), 7.46–7.49 (m, 2H), 7.26 (s, 1H), 7.15–7.19 (m, 2H), 7.07 (s, 1H), 4.95–4.99 (m, 1H), 4.45–4.47 (m, 2H), 4.15–4.18 (m, 2H), 3.77–3.82 (m, 7H), 3.54–3.62 (m, 9H), 2.45–2.77 (m, 3H), 1.91–1.95 (m, 1H), 1.12–1.16 (m, 1H).                                                                                                                                                                                                                                                           |
| 70 |   | A | 778.5 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 11.10 (s, 1H), 9.36 (s, 1H), 8.62 (s, 1H), 8.50 (s, 1H), 8.31 (d, <i>J</i> = 8.2 Hz, 1H), 8.18 (d, <i>J</i> = 8.8 Hz, 1H), 7.97 (s, 1H), 7.81 (d, <i>J</i> = 8.3 Hz, 1H), 7.60 (d, <i>J</i> = 8.0 Hz, 2H), 7.43 (s, 1H), 7.35 (d, <i>J</i> = 7.8 Hz, 1H), 6.93 (d, <i>J</i> = 8.7 Hz, 1H), 5.31 (s, 1H), 5.11 (dd, <i>J</i> = 12.8, 5.1 Hz, 1H), 4.31 (s, 2H), 4.22 (s, 1H), 3.95 (s, 3H), 3.79 (s, 2H), 3.64–3.48 (m, 10H), 3.45 (d, <i>J</i> = 4.9 Hz, 3H), 2.86 (d, <i>J</i> = 13.2 Hz, 1H), 2.45–2.40 (m, 2H), 2.37–2.30 (m, 2H), 2.02 (d, <i>J</i> = 6.5 Hz, 1H). |
| 71 |  | A | 746.5 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 9.39 (s, 1H), 8.38 (d, <i>J</i> = 8.4 Hz, 1H), 8.30 (d, <i>J</i> = 2.0 Hz, 1H), 8.28 (d, <i>J</i> = 3.0 Hz, 1H), 8.11 (s, 1H), 7.80 (d, <i>J</i> = 8.4 Hz, 1H), 7.72 (d, <i>J</i> = 7.6 Hz, 1H), 7.63–7.68 (m, 2H), 7.44 (d, <i>J</i> = 2.0 Hz, 1H), 7.34–7.36 (m, 1H), 5.08–5.12 (m, 1H), 4.48 (s, 2H), 4.31 (t, <i>J</i> = 3.6 Hz, 2H), 3.98 (s, 3H), 3.80 (s, 3H), 3.53–3.79 (m, 12H), 1.95–2.08 (m, 2H).                                                                                                                                                           |
| 72 |  | C | 792.5 | <sup>1</sup> H NMR(400 MHz, CD <sub>3</sub> OD): δ 13.19 (s, 1H), 9.77 (s, 1H), 8.62–8.68 (m, 2H), 8.52 (d, <i>J</i> = 8.0 Hz, 1H), 8.16 (s, 1H), 8.01–8.02 (m, 2H), 7.80–7.81 (m, 1H), 7.15–7.28 (m, 1H), 6.99 (d, <i>J</i> = 8.0 Hz, 1H), 5.15–5.23 (m, 1H), 4.43–4.45 (m, 2H), 3.77–3.89 (m, 4H), 3.49–3.60 (m, 12H), 2.86–3.05 (m, 3H), 1.99–2.01 (m, 1H).                                                                                                                                                                                                                                                                       |

|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|----|-------------------------------------------------------------------------------------|---|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 73 |    | A | 719.4 | <sup>1</sup> H NMR (400 MHz, DMSOd-6): δ 2.04-2.07 (m, 1H), 2.57-2.77 (m, 6H), 2.86-2.93 (m, 1H), 5.10-5.14 (m, 2H), 5.32 (s, 2H), 5.39-5.48 (m, 1H), 6.97 (d, <i>J</i> = 8.0 Hz, 1H), 7.32-7.33 (m, 1H), 7.46-7.58 (m, 5H), 7.77 (s, 1H), 7.90 (d, <i>J</i> = 7.2 Hz, 1H), 8.14 (d, <i>J</i> = 7.2 Hz, 1H), 8.25 (s, 1H), 8.30 (d, <i>J</i> = 7.6 Hz, 1H), 8.43 (s, 1H), 8.56 (s, 1H), 9.36 (s, 1H), 11.12 (s, 1H), 11.82 (s, 1H).                                                                                                                                                    |
| 74 |   | A | 750.5 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 9.65 (s, 1H), 9.22 (s, 1H), 8.67–8.73 (m, 2H), 8.47 (d, <i>J</i> = 7.6 Hz, 1H), 8.36 (d, <i>J</i> = 8.0 Hz, 1H), 7.97 (s, 1 H), 7.83 (s, 1H), 7.81(s, 1H), 7.59–7.71 (m, 2H), 7.04 (d, <i>J</i> = 9.2 Hz, 2H), 4.93–4.96 (m, 1H), 4.10 (s, 5H), 3.87 (s, 1H), 3.55–3.76 (m, 18H), 3.26 (s, 2H), 2.12–2.16 (m, 2H).                                                                                                                                                                                                                 |
| 75 |  | C | 771.6 | <sup>1</sup> H NMR (400MHz, DMSO-d <sub>6</sub> )<br>δ = 11.07 (s, 1H), 9.38 - 9.32 (m, 1H), 8.66 - 8.63 (d, <i>J</i> = 12 Hz 1H), 8.50 - 8.48 (m, <i>J</i> = 8 Hz 1H), 8.36 (s, 2H), 8.34 - 8.29 (m, 1H), 8.21 - 8.14 (m, 1H), 7.99 - 7.94 (m, 1H), 7.61 (s, 3H), 7.28 - 7.22 (m, 1H), 7.19 - 7.12 (m, 1H), 6.96 - 6.89 (m, 1H), 5.09 - 5.00 (m, 1H), 4.36 - 4.29 (m, 2H), 3.95 (s, 5H), 3.34 (s, 4H), 2.87 (s, 2H), 2.99 - 2.78 (m, 1H), 2.82 - 2.73 (m, 1H), 2.04 - 1.93 (m, 1H), 1.82 - 1.65 (m, 4H), 1.61 - 1.52 (m, 2H), 1.52 - 1.41 (m, 5H), 1.28 (s, 4H), 1.22 - 1.05 (m, 4H). |
| 76 |  | C | 751.5 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.32 (s, 1H), 8.96 (s, 1H), 8.45-8.52 (m, 2H), 8.37 (d, <i>J</i> = 8.0 Hz, 1H), 8.27-8.31(m, 1H), 7.98 (s, 1H), 7.61-7.98 (m, 4H), 6.82 (s, 1H), 6.65-6.67 (m, 1H), 5.01-5.05 (m, 1H), 4.59 (m, 1H), 4.27 (t, <i>J</i> = 8.4 Hz, 1H), 4.02 (s, 3H), 3.88-3.91 (m, 2H), 3.70 (s, 2H), 3.57(t, <i>J</i> = 6.0 Hz, 2H), 3.41(m, 1H), 3.13-3.17 (m, 2H), 2.66-2.86 (m, 11H), 2.02-2.03 (m, 3H).                                                                                                                                        |

|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|----|-------------------------------------------------------------------------------------|---|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 77 |    | C | 723.5 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): $\delta$ 9.56 (s, 1H), 8.54–8.56 (m, 2H), 8.45 (d, $J$ = 8.4 Hz, 1H), 8.37 (d, $J$ = 2.4 Hz, 1H), 8.13 (d, $J$ = 8.0 Hz, 1H), 7.97 (d, $J$ = 8.0 Hz, 1H), 7.88 (d, $J$ = 8.8 Hz, 2H), 7.81 (d, $J$ = 8.4 Hz, 1H), 7.79 (s, 1H), 7.76–7.78 (d, $J$ = 8 Hz, 1H), 7.29 (s, 1H), 7.21 (d, $J$ = 8.0 Hz, 1H), 6.98 (d, $J$ = 8.0 Hz, 1H), 5.48–5.52 (m, 1H), 5.32–5.34 (m, 1H), 5.18–5.22 (m, 1H), 5.06–5.10 (m, 1H), 4.25–4.28 (m, 2H), 3.21–3.23 (m, 3H), 2.78–2.81 (m, 5H), 2.67–2.70 (m, 2H), 2.30–2.33 (m, 2H), 2.17–2.19 (m, 1H), 1.97–2.07 (m, 3H).                |
| 78 |  | C | 770.6 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): $\delta$ 11.08 (s, 1H), 9.35 (s, 1H), 8.64 (t, $J$ = 3.9 Hz, 1H), 8.64 (t, $J$ = 3.9 Hz, 1H), 8.49 (d, $J$ = 4.7 Hz, 1H), 8.32 (d, $J$ = 8.1 Hz, 1H), 8.19 (dd, $J$ = 8.6, 2.5 Hz, 1H), 7.98 (s, 1H), 7.68–7.48 (m, 3H), 7.31 (d, $J$ = 7.8 Hz, 1H), 7.20 (t, $J$ = 9.5 Hz, 1H), 6.94 (d, $J$ = 8.6 Hz, 1H), 5.07 (dd, $J$ = 12.9, 5.3 Hz, 1H), 4.33 (t, $J$ = 6.5 Hz, 2H), 3.95 (s, 3H), 3.65 (m, 1H), 3.51–3.41 (m, 3H), 3.36–3.23 (m, 5H), 2.95–2.83 (m, 1H), 2.43–2.28 (m, 6H), 2.05–1.96 (m, 1H), 1.79–1.73 (m, 1H), 1.67–1.61 (m, 1H), 1.42 (m, 7H). |
| 79 |  | A | 759.6 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): $\delta$ 9.35 (s, 1H), 8.59 (d, $J$ = 5.7 Hz, 1H), 8.49 (s, 1H), 8.28 (s, 1H), 8.21 (d, $J$ = 10.6 Hz, 1H), 8.00 (s, 1H), 7.91 (d, $J$ = 11.0 Hz, 1H), 7.63 (d, $J$ = 8.2 Hz, 1H), 7.57 (s, 1H), 7.51 (d, $J$ = 9.3 Hz, 1H), 7.37 (d, $J$ = 5.9 Hz, 1H), 6.85 (d, $J$ = 8.6 Hz, 1H), 6.77 (s, 1H), 4.92 (m, 1H), 4.45 (s, 1H), 4.36 (t, $J$ = 6.6 Hz, 2H), 4.16–4.26 (m, 2H), 3.83–3.98 (m, 4H), 3.44 (m, 4H), 2.63–2.92 (m, 3H), 2.11 (d, $J$ = 6.4 Hz, 2H), 1.79–1.89 (m, 3H), 1.44–1.70 (m, 10H).                                                                 |
| 80 |  | A | 759.6 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): $\delta$ 11.12 (s, 1H), 9.35 (s, 1H), 8.63 (d, $J$ = 2.3 Hz, 1H), 8.50 (s, 1H), 8.31 (d, $J$ = 8.1 Hz, 1H), 8.18 (dd, $J$ = 8.6, 2.5 Hz, 1H), 7.96 (s, 1H),                                                                                                                                                                                                                                                                                                                                                                                                |



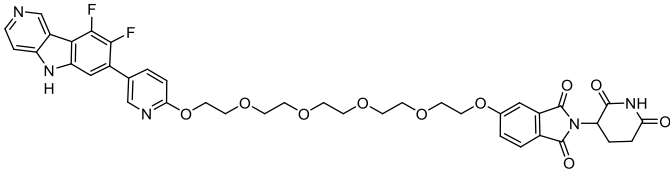
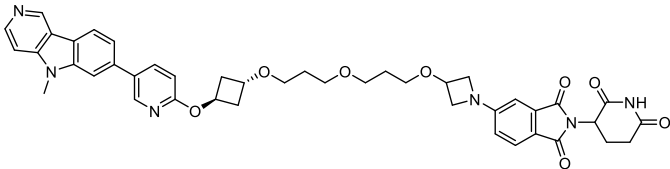
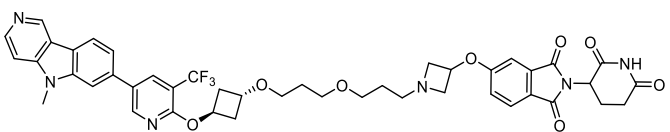
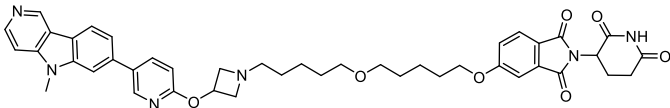
|    |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|----|-------------------------------------------------------------------------------------|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 84 |    | C | 794.5 | <sup>1</sup> H NMR(400 MHz, CDCl <sub>3</sub> ):<br>$\delta$ 9.34 (s, 1H), 8.58 (d, $J$ = 5.6 Hz, 1H), 8.21-8.48 (m, 2H), 8.20 (d, $J$ = 8.4 Hz, 1H), 7.88-7.91 (m, 1H), 7.76 (d, $J$ = 8.4 Hz, 1H), 7.56 (s, 1H), 7.51 (d, $J$ = 8.0 Hz, 1H), 7.33-7.36 (m, 2H), 7.16-7.18 (m, 2H), 6.86 (d, $J$ = 8.4 Hz, 1H), 6.39-6.51 (m, 3H), 5.52-5.54 (m, 1H), 4.94-4.96 (m, 2H), 4.07-4.10 (m, 2H), 3.91-3.97 (m, 5H), 3.22-3.24 (m, 1H), 2.69-2.76 (m, 7H), 2.14-2.16 (m, 1H), 1.82-1.86 (m, 4H), 1.54-1.57 (m, 4H).                                                                                |
| 85 |  | A | 774.6 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ):<br>$\delta$ 9.32 (s, 1H), 8.58–8.59 (d, $J$ = 4.0 Hz, 2H), 8.48 (s, 1H), 8.16–8.18 (d, $J$ = 8.0 Hz, 1H), 7.89–7.91(d, $J$ = 8.0 Hz, 1H), 7.74–7.76 (d, $J$ = 8.0 Hz, 1H), 7.56 (s, 1H), 7.47–7.49 (d, $J$ = 8.0 Hz, 1H), 7.32–7.33 (d, $J$ = 4.0 Hz, 1H), 7.19 (s, 1H), 7.06–7.08 (d, $J$ = 8.0 Hz, 1H), 6.84–6.86 (d, $J$ = 8.0 Hz, 1H), 4.93 (m, 2H), 4.35–4.38 (m, 2H), 4.21 (s, 1H), 3.90 (s, 3H), 3.35–3.49 (m, 7H), 2.68–2.95 (m, 3H), 2.44–2.51 (m, 4H), 2.15 (m, 1H), 1.88 (m, 2H), 1.56–1.68 (m, 9H), 1.44 (d, $J$ = 8.0 Hz, 2H). |
| 86 |  | C | 736.5 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ):<br>$\delta$ 9.28 (s, 2H), 8.50 (s, 1H), 8.08 (s, 1H), 7.35–7.57 (m, 6H), 6.94–6.96 (m, 3H), 6.77 (s, 1H), 6.38 (s, 1H), 4.88–4.90 (m, 1H), 4.14 (s, 2H), 3.60–3.86 (m, 17H), 3.31–3.34 (m, 2H), 2.66–2.86 (m, 3H), 2.03–2.05 (m, 1H).                                                                                                                                                                                                                                                                                                       |
| 87 |  | C | 739.5 | <sup>1</sup> H NMR(400 MHz, CDCl <sub>3</sub> ):<br>$\delta$ 9.28 (s, 1H), 8.42 (s, 1H), 8.37–8.39 (m, 2H), 8.06 (d, $J$ = 8.0 Hz, 1H), 7.80 (d, $J$ = 8.0 Hz, 1H), 7.62 (s, 1H), 7.40–7.45 (m, 3H), 6.09 (s, 1H), 6.82 (d, $J$ = 8.8 Hz, 1H), 4.94–4.99 (m, 1H), 4.54 (t, $J$ = 4.8 Hz, 4H), 3.86–3.91 (m, 4H), 3.66–3.75 (m, 12H), 2.73–2.92 (m, 3H), 2.20–2.22 (m, 1H).                                                                                                                                                                                                                    |

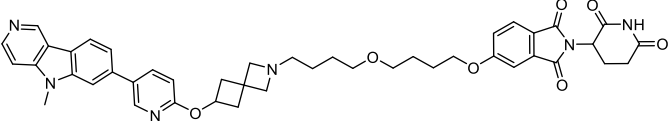
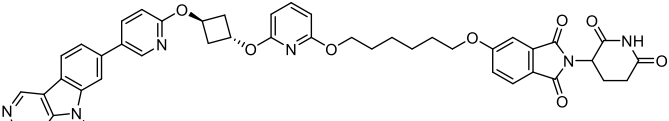
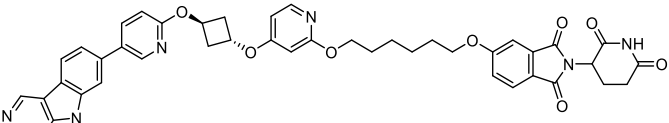


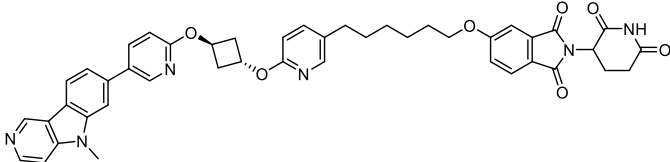
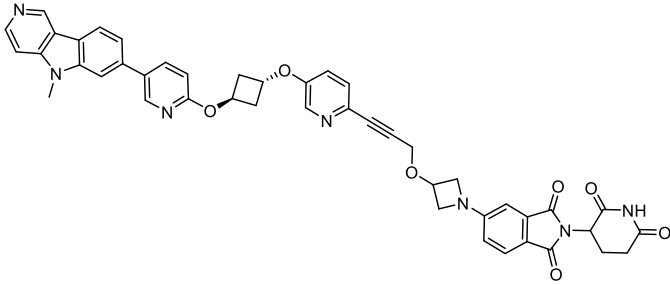
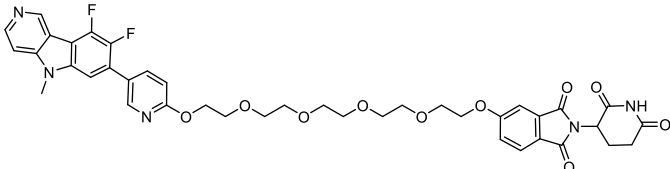
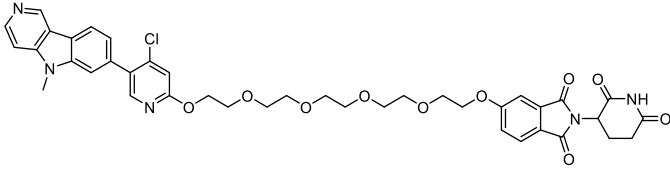
|    |  |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|----|--|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 92 |  | A | 786.5 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 9.32 (s, 1H), 8.68 (s, 1H), 8.58 (s, 1H), 8.35 (s, 1H), 8.18 (d, <i>J</i> = 8.0 Hz, 1H), 7.97 (s, 1H), 7.74 (d, <i>J</i> = 8.4 Hz, 1H), 7.52 (s, 1H), 7.45 (d, <i>J</i> = 8.0 Hz, 1H), 7.27–7.34 (m, 2H), 7.20 (d, <i>J</i> = 7.6 Hz, 1H), 4.92–4.96 (m, 1H), 4.61 (s, 2H), 4.23 (s, 2H), 3.89–3.94 (m, 8H), 3.68–3.78 (m, 11H), 2.72–2.90 (m, 3H), 2.01–2.12 (m, 1H).                                                                                                                                                                          |
| 93 |  | C | 782.5 | <sup>1</sup> H NMR(400 MHz, CDCl <sub>3</sub> ): δ 9.35 (br, 1H), 8.94 (s, 1H), 8.59(s, 1H), 8.21 (d, <i>J</i> = 8.0 Hz, 1H), 8.01-8.09(m, 2H), 7.73 (d, <i>J</i> = 8.4 Hz, 1H), 7.69 (d, <i>J</i> = 8.0 Hz, 1H), 7.58 (s, 1H), 7.51(d, <i>J</i> = 8.4 Hz, 1H), 7.31(d, <i>J</i> = 5.2 Hz, 1H), 7.24(s, 1H), 7.09(dd, <i>J</i> = 8.0, 2.0 Hz, 1H), 4.85-4.90 (m, 1H), 4.10(t, <i>J</i> = 8.0 Hz, 1H), 3.98(t, <i>J</i> = 6.4 Hz, 1H), 3.87(s, 3H), 3.51 (t, <i>J</i> = 6.4 Hz, 1H), 3.27-3.32 (m, 4H), 2.65-2.85(m, 3H), 2.04-2.08 (m, 1H), 1.71-1.76 (m, 4H), 1.45-1.52 (m, 8H), 0.75-0.85(m, 4H). |
| 94 |  | C | 761.5 | <sup>1</sup> HNMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ: 11.04(s, 1H), 9.29(s, 1H), 8.58(d, <i>J</i> = 2.0 Hz, 1H), 8.43(d, <i>J</i> = 5.6 Hz, 1H), 8.25(d, <i>J</i> = 8.0 Hz, 1H), 8.12-8.16(m, 2H), 7.92(s, 1H), 7.78(d, <i>J</i> = 7.6 Hz, 1H), 7.56(d, <i>J</i> = 6.0 Hz, 2H), 7.40(s, 1H), 7.33(d, <i>J</i> = 8.4 Hz, 2H), 7.20-7.22(m, 1H), 6.92(d, <i>J</i> = 4.4 Hz, 1H), 5.37(s, 1H), 5.01-5.37(m, 2H), 4.25(t, <i>J</i> = 6.0 Hz, 2H), 3.89(s, 3H), 2.43-2.65(m, 9H), 1.98(t, <i>J</i> = 6.4 Hz, 3H).                                                                                |
| 95 |  | C | 765.5 | <sup>1</sup> HNMR (400 MHz, CDCl <sub>3</sub> ): δ: 9.32(s, 1H), 8.59(d, <i>J</i> = 4.8 Hz, 1H), 8.49(s, 1H), 8.20(d, <i>J</i> = 8.8 Hz, 1H), 8.16(s, 1H), 8.08(s, 1H), 7.94(d, <i>J</i> = 7.2 Hz, 1H), 7.77(d, <i>J</i> = 8.0 Hz, 1H), 7.56(s, 1H), 7.49(d, <i>J</i> = 8.4 Hz, 1H), 7.32(s, 2H), 7.17(d, <i>J</i> = 8.0 Hz, 1H), 7.07(s, 1H), 6.87(d, <i>J</i> = 8.8 Hz, 1H), 5.52(s, 1H), 4.94-4.97(m, 2H), 4.08(s, 2H), 3.91(s, 3H), 2.73-2.92(m, 8H), 2.13-2.15(m, 2H), 1.86-1.88(m, 2H), 1.78-1.80(m,                                                                                          |

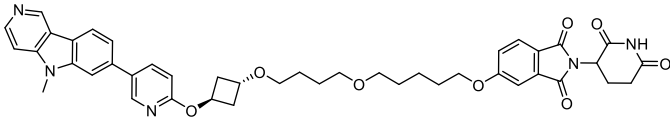
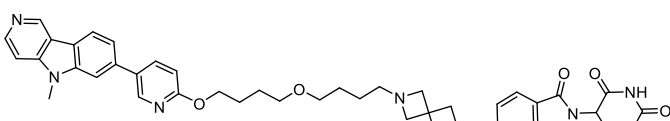


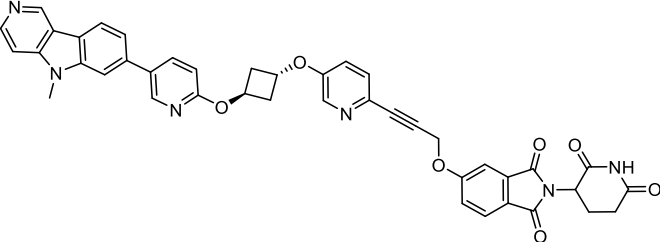
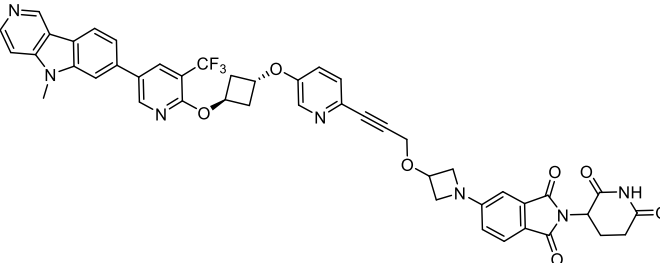
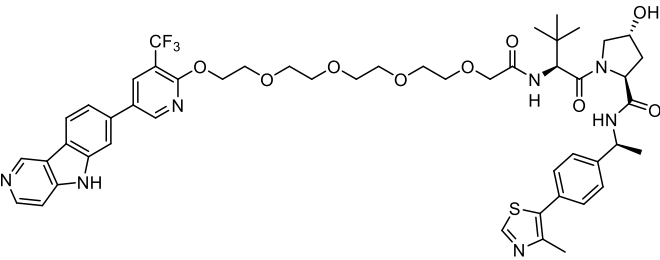
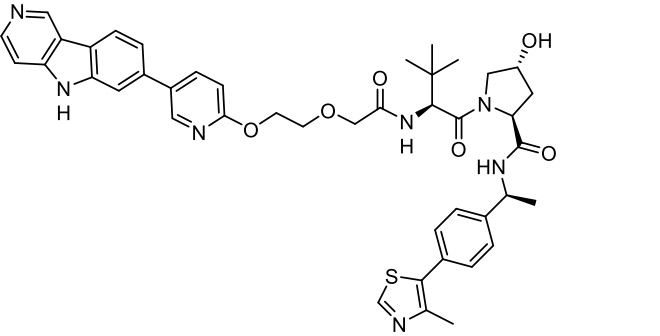


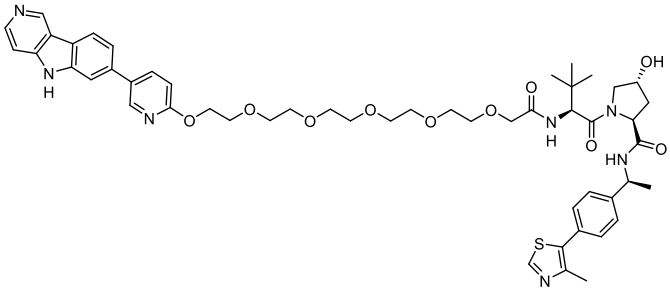
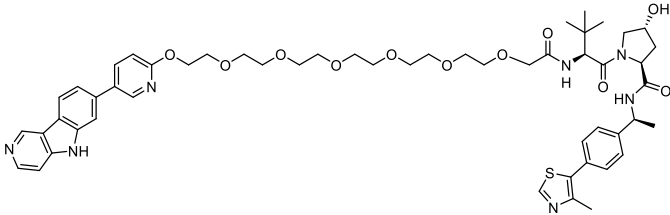
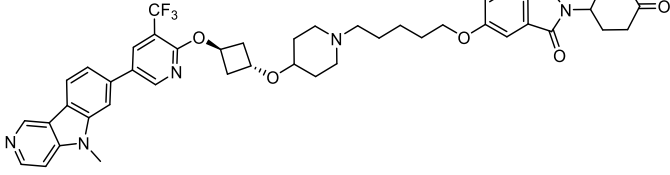
|     |                                                                                     |    |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|-----|-------------------------------------------------------------------------------------|----|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |    |       | 1H), 8.64 (d, <i>J</i> = 1.6 Hz, 1H), 9.40 (s, 1H),11.11 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| 103 |    | ND | 774.5 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 9.46 (s, 1H), 8.63 (d, <i>J</i> = 6.8 Hz, 1H), 8.38 (s, 1H), 8.00 (d, <i>J</i> = 6.8 Hz, 1H), 7.96 (d, <i>J</i> = 8.8 Hz, 1H), 7.67 (d, <i>J</i> = 8.4 Hz, 1H), 7.61 (d, <i>J</i> = 4.8 Hz, 1H), 7.29 (s, 1H), 7.23 (d, <i>J</i> = 8.4 Hz, 1H), 6.93 (d, <i>J</i> = 8.8 Hz, 1H), 5.05 (m, 1H), 4.54 – 4.45 (m, 2H), 4.26 – 4.19 (m, 2H), 3.86 (m, 4H), 3.70-3.65 (m, 12H), 2.86 – 2.62 (m, 3H), 2.10 – 2.04 (m, 1H).                                                                                                                                         |
| 104 |  | A  | 773.5 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 1.73-1.79 (m, 4H), 1.97-1.99 (m, 2H), 2.31-2.37 (m, 2H), 2.40-2.49 (m, 2H), 2.54-2.59 (m, 1H), 2.83-2.88 (m, 1H), 3.38 (t, <i>J</i> = 6.4 Hz, 2H), 3.43-3.49 (m, 6H), 3.82-3.85 (m, 2H), 3.75 (s, 3H), 4.16-4.18 (m, 1H), 4.20-4.26 (m, 2H), 4.43-4.47 (m, 1H), 5.02-5.07 (m, 1H), 5.31-5.34 (m, 1H), 6.62-6.64 (m, 1H), 6.78-6.79 (m, 1H), 6.93 (t, <i>J</i> = 8.4 Hz, 1H), 7.59-6.72 (m, 3H), 7.96 (s, 1H), 8.17-8.19 (m, 1H), 8.30 (d, <i>J</i> = 8.0 Hz, 1H), 8.49 (d, <i>J</i> = 6.4 Hz, 1H), 8.62-8.63 (m, 1H), 9.35 (s, 1H), 11.06 (s, 1H). |
| 105 |  | A  | 841.5 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 1.56-1.60 (m, 2H), 1.74 (t, <i>J</i> = 6.4 Hz, 2H), 1.99-2.04 (m, 2H), 2.33-2.39 (m, 3H), 2.55-2.66 (m, 3H), 2.83-2.91 (m, 1H), 3.11-3.13 (m, 2H), 3.36-3.44 (m, 6H), 3.55-3.64 (m, 2H), 3.88-3.93 (m, 1H), 3.97 (s, 3H), 4.17-4.20 (m, 1H), 5.06-5.12 (m, 2H), 5.47-5.49 (m, 1H), 7.27 (s, 2H), 7.65 (d, <i>J</i> = 6.0 Hz, 1H), 7.70 (d, <i>J</i> = 8.4 Hz, 1H), 7.80 (d, <i>J</i> = 8.0 Hz, 1H), 8.10 (s, 1H), 8.35 (s, 1H), 8.50-8.53 (m, 2H), 8.90 (s, 1H), 9.40 (s, 1H), 11.10 (s, 1H).                                                      |
| 106 |  | B  | 759.6 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 1.54-1.68 (m, 10H), 1.84-1.88 (m, 2H), 2.12-2.14 (m, 1H), 2.77-2.93 (m, 5H), 3.40-3.45 (m, 4H), 3.64-3.75 (m, 4H), 3.91 (s, 3H), 4.09 (t, <i>J</i> = 6.4 Hz, 2H), 4.39-4.46 (m, 1H), 4.89-4.99 (m, 1H), 5.41-5.50 (m, 1H), 6.90 (d, <i>J</i>                                                                                                                                                                                                                                                                                                       |

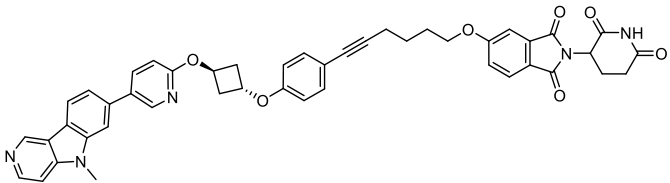
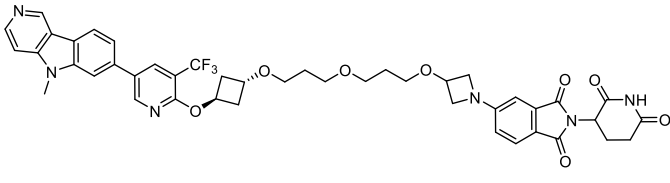
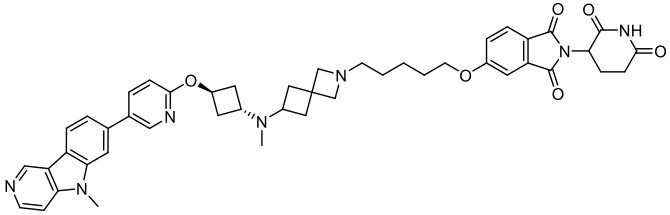
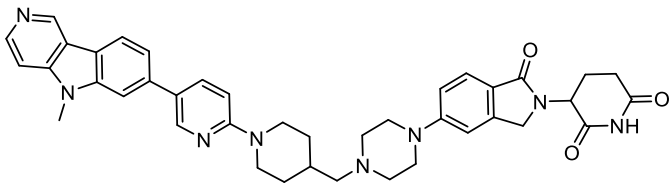
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-----|-------------------------------------------------------------------------------------|---|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | = 8.4 Hz, 1H), 7.14-7.2 (m, 1H), 7.32-7.35 (m, 2H), 7.48 (d, <i>J</i> = 8.0 Hz, 1H), 7.55 (s, 1H), 7.76 (d, <i>J</i> = 8.0 Hz, 1H), 7.92-8.00 (m, 1H), 8.21 (d, <i>J</i> = 8.0 Hz, 1H), 8.43 (d, <i>J</i> = 2.0 Hz, 1H), 8.59 (d, <i>J</i> = 5.6 Hz, 1H), 9.33 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                        |
| 107 |    | C | 771.6 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 1.61-1.65 (m, 2H), 1.72-1.77 (m, 4H), 1.90-1.93 (m, 2H), 1.99-2.04 (m, 1H), 2.14-2.22 (m, 3H), 2.44-2.49 (m, 2H), 2.78-3.01 (m, 6H), 3.44-3.49 (m, 4H), 3.92 (s, 3H), 3.99-4.05 (m, 2H), 4.14 (t, <i>J</i> = 6.2 Hz, 2H), 4.94-4.98 (m, 1H), 5.17-5.20 (m, 1H), 6.81 (d, <i>J</i> = 8.4 Hz, 1H), 7.19-7.21 (m, 1H), 7.33-7.37 (m, 2H), 7.49 (d, <i>J</i> = 8.4 Hz, 1H), 7.56 (s, 1H), 7.78 (d, <i>J</i> = 8.4 Hz, 1H), 7.90-7.93 (m, 1H), 8.21 (d, <i>J</i> = 8.4 Hz, 1H), 8.35 (br, 1H), 8.45-8.46 (m, 1H), 8.59 (d, <i>J</i> = 5.6 Hz, 1H), 9.34(s, 1H).                                                                 |
| 108 |  | C | 795.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.43-1.44 (m, 4H), 1.70-1.74 (m, 4H), 1.98-2.04 (m, 1H), 2.44-2.47 (m, 1H), 2.56-2.60 (m, 1H), 2.65 (t, <i>J</i> = 6.0 Hz, 4H), 2.83-2.92 (m, 1H), 3.95 (s, 3H), 4.10 (t, <i>J</i> = 6.0 Hz, 2H), 4.22 (t, <i>J</i> = 6.4 Hz, 2H), 5.07-5.11 (m, 1H), 5.30-5.35 (m, 1H), 5.39-5.45 (m, 1H), 6.34-6.37 (m, 2H), 6.98 (d, <i>J</i> = 8.4 Hz, 1H), 7.24-7.26 (m, 1H), 7.33 (d, <i>J</i> = 2.0 Hz, 1H), 7.59-7.65 (m, 3H), 7.72 (d, <i>J</i> = 8.0 Hz, 1H), 7.97 (s, 1H), 8.17-8.21 (m, 1H), 8.31 (d, <i>J</i> = 8.0 Hz, 1H), 8.50 (d, <i>J</i> = 6.0 Hz, 1H), 8.65 (d, <i>J</i> = 2.0 Hz, 1H), 9.36 (s, 1H), 11.10 (s, 1H). |
| 109 |  | C | 795.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.47 (s, 4H), 1.72-1.78 (m, 4H), 2.02-2.05 (m, 2H), 2.33 (s, 1H), 2.63-2.66 (m, 4H), 2.88-2.89 (m, 1H), 3.41-3.49 (m, 2H), 3.96 (s, 2H), 4.18-4.23 (m, 3H), 5.04-5.12 (m, 2H), 5.42 (br, 1H), 6.19 (s, 1H), 6.55-6.56 (m, 1H), 6.98 (d, <i>J</i> = 8.4 Hz, 1H), 7.34(d, <i>J</i> = 7.2 Hz, 1H), 7.41 (s, 1H), 6.63(s, 2H), 7.81-7.83 (m, 1H), 7.95-7.97 (m, 2H), 8.21 (d, <i>J</i> = 8.4 Hz, 1H), 8.32 (d, <i>J</i> =                                                                                                                                                                                                    |

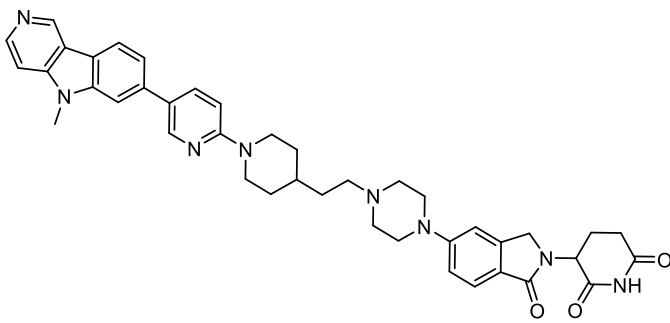
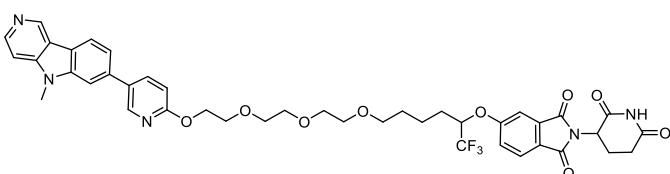
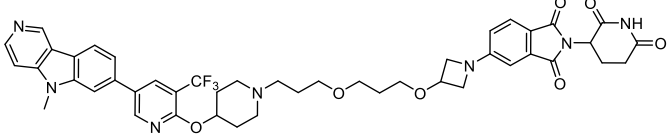
|     |                                                                                     |   |                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-----|-------------------------------------------------------------------------------------|---|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |                  | 7.2 Hz, 1H), 8.50 (d, $J$ = 4.0 Hz, 1H), 8.64 (s, 1H), 9.36 (s, 1H), 11.11 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 110 |    | C | 779.5            | <sup>1</sup> H NMR (400 MHz,DMSO- <i>d</i> <sub>6</sub> ): δ 1.36 (d, $J$ = 7.6 Hz, 2H), 1.45 (d, $J$ =6.8 Hz, 2H), 1.52-1.61 (m, 2H), 1.70-1.80 (m, 2H), 1.98-2.02 (m, 3H), 2.54-2.70 (m, 6H), 2.89 (t, $J$ = 16.6 Hz, 1H), 3.96 (s, 3H), 4.16 (d, $J$ = 5.0 Hz, 2H), 5.12 (dd, $J$ = 12.8, 4.4 Hz, 1H), 5.36-5.43 (m, 2H), 6.77 (d, $J$ = 8.4 Hz, 1H), 6.99 (d, $J$ = 8.0 Hz, 1H),7.34 (d, $J$ = 8.8 Hz, 1H), 7.42 (s, 1H),7.60-7.64 (m, 3H), 7.83 (d, $J$ = 8.0 Hz, 1H), 7.97 (dd, $J$ = 14.0, 6.4 Hz, 2H), 8.33 (d, $J$ = 8.4 Hz, 1H), 8.21 (d, $J$ = 8.0 Hz, 1H), 8.50 (d, $J$ = 4.8 Hz, 1H), 8.65 (s, 1H), 9.37 (s, 1H), 11.11 (s, 1H). |
| 111 |  | C | 788.5            | <sup>1</sup> HNMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 1.98-2.02 (m, 1H), 2.54-2.73 (m, 6H), 2.83-2.92 (m, 1H), 3.95-3.97 (m, 5H), 4.31-4.34 (m, 2H), 4.50 (s, 2H), 4.67-4.72 (m, 1H), 5.04-5.13 (m, 2H), 5.42-5.48 (m, 1H), 6.67-6.69 (m, 1H), 6.82 (s, 1H), 6.69-7.01 (m, 1H), 7.33-7.36 (m, 1H), 7.53-7.55 (m, 1H), 7.63-7.67 (m, 3H), 8.01 (s, 1H), 8.21-8.26 (m, 2H), 8.33-8.37 (m, 1H), 8.51-8.55 (m, 1H), 8.65-8.66 (m, 1H), 9.39 (s, 1H), 11.07 (s, 1H).                                                                                                                                                                        |
| 112 |  | A | 788.5            | <sup>1</sup> HNMR (400 MHz, CDCl <sub>3</sub> ): δ: 11.09(s, 1H), 9.25(s, 1H), 8.50(s, 1H), 8.59(s, 1H), 8.07(d, $J$ = 8.4 Hz, 1H), 7.79(d, $J$ = 8.4 Hz, 1H), 7.69-7.73(m, 2H), 7.75(d, $J$ = 8.4 Hz, 1H), 7.42(s, 1H), 7.34(d, $J$ = 8.4 Hz, 1H), 7.02(d, $J$ = 8.4 Hz, 1H), 5.08-5.13(m, 1H), 4.46(d, $J$ = 4.4 Hz, 2H), 4.30-4.34(m, 2H), 3.95(s, 3H), 3.79(s, 4H), 3.60(s, 4H), 3.56(s, 4H), 3.53(s, 4H), 2.85-2.88(m, 1H), 2.61(s, 2H).                                                                                                                                                                                                 |
| 113 |  | C | 786.5<br>[788.5] | <sup>1</sup> HNMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 11.11 (s, 1H), 9.35 (s, 1H), 8.50 (s, 1H), 8.38 (s, 1H), 8.29 (d, $J$ = 8.0 Hz, 1H), 7.87 (s, 1H), 7.75 (d, $J$ = 8.0 Hz, 1H), 7.62 (d, $J$ = 5.6 Hz, 1H), 7.52 (d, $J$ = 8.0 Hz, 1H), 7.34 (d, $J$ = 8.4 Hz, 2H), 7.27                                                                                                                                                                                                                                                                                                                                                          |

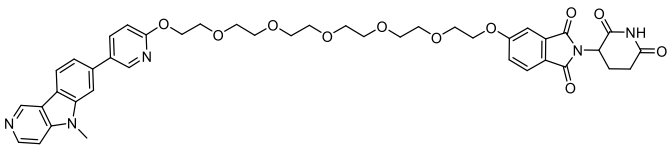
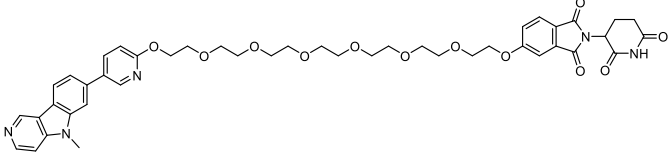
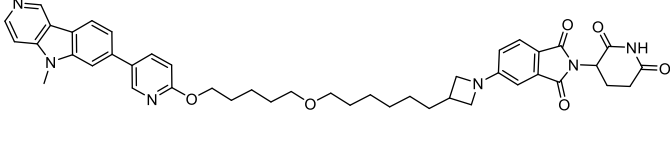
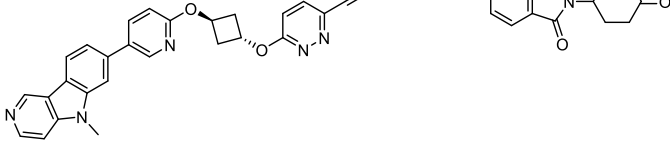
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-----|-------------------------------------------------------------------------------------|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | (d, $J$ = 10.4 Hz, 1H), 5.13-5.08 (m, 1H), 4.34-4.32 (m, 2H), 4.23-4.21 (m, 2H), 3.91 (s, 3H), 3.77-3.71 (m, 4H), 3.54-3.46 (m, 12 H), 2.91-2.87 (m, 1H), 2.61-2.57 (m, 3H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| 114 |    | C | 760.5 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 1.52-1.59 (m, 2H), 1.63-1.67 (m, 5H), 1.83-1.90 (m, 1H), 2.11-2.16 (m, 2H), 2.43-2.54 (m, 4H), 2.71-2.92 (m, 4H), 3.39-3.49 (m, 6H), 3.95 (s, 3H), 4.08 (t, $J$ = 6.4 Hz, 2H), 4.23-4.29 (m, 1H), 4.94 (dd, $J$ = 5.2, 12.0 Hz, 1H), 6.83 (d, $J$ = 8.4 Hz, 1H), 7.17 (dd, $J$ = 2.0, 8.0 Hz, 1H), 7.32 (d, $J$ = 1.6 Hz, 1H), 7.44 (d, $J$ = 6.0 Hz, 1H), 7.54 (d, $J$ = 8.0 Hz, 1H), 7.60 (s, 1H), 7.75 (d, $J$ = 8.4 Hz, 1H), 7.91 (dd, $J$ = 2.4, 8.8 Hz, 1H), 8.14 (m, 1H), 8.21 (d, $J$ = 8.0 Hz, 1H), 8.48 (d, $J$ = 2.4 Hz, 1H), 8.58 (d, $J$ = 5.2 Hz, 1H), 9.34 (s, 1H).        |
| 115 |  | C | 759.6 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.34-1.38 (m, 2H), 1.40-1.58 (m, 8H), 1.74-1.77 (m, 2H), 2.01-2.04 (m, 1H), 2.54-2.61 (m, 1H), 2.84-2.93 (m, 1H), 3.32-3.42 (m, 7H), 3.77-3.81 (m, 2H), 3.96 (s, 3H), 4.15 (t, $J$ = 6.4 Hz, 2H), 4.21 (t, $J$ = 8.8 Hz, 2H), 4.40-4.45 (m, 1H), 5.10 (dd, $J$ = 12.8 Hz, 1H), 6.52 (d, $J$ = 8.8 Hz, 1H), 7.32 (dd, $J$ = 8.0 Hz, 1H), 7.39 (s, 1H), 7.58 (d, $J$ = 8.0 Hz, 1H), 7.65 (d, $J$ = 6.0 Hz, 1H), 7.80 (d, $J$ = 8.4 Hz, 1H), 7.91 (s, 1H), 8.01 (dd, $J$ = 8.4 Hz, 1H), 8.29 (d, $J$ = 8.0 Hz, 1H), 8.50 (d, $J$ = 5.6 Hz, 1H), 8.58 (s, 1H), 9.36 (s, 1H), 11.10 (s, 1H). |
| 116 |  | C | 771.6 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 1.39-1.42 (m, 2H), 1.47-1.52 (m, 2H), 1.64-1.70 (m, 2H), 1.77-1.82 (m, 2H), 2.01-2.07 (m, 1H), 2.21-2.26 (m, 2H), 2.54-2.64 (m, 3H), 2.75-2.90 (m, 5H), 3.42-3.45 (m, 3H), 3.61-3.71 (m, 4H), 3.95 (s, 3H), 4.35 (t, $J$ = 6.2 Hz, 2H), 4.78-4.82 (m, 1H), 5.09-5.13 (m, 1H), 6.94 (d, $J$ = 8.4 Hz, 1H), 7.20-7.25 (m, 2H), 7.60-7.63 (m, 2H), 7.79 (d, $J$ = 8.0 Hz, 1H), 7.97 (s, 1H), 8.18-8.20 (m, 1H), 8.31                                                                                                                                                                         |

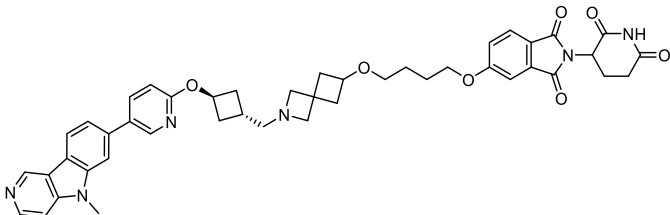
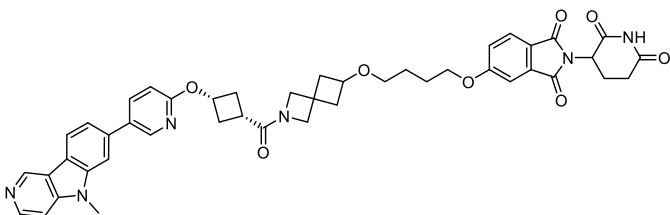
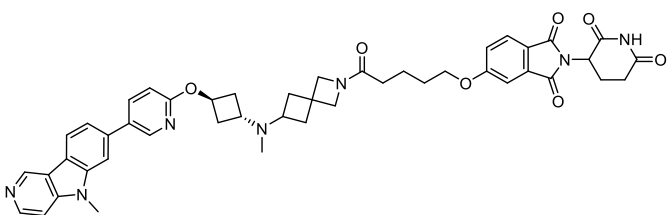
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-----|-------------------------------------------------------------------------------------|---|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | (d, $J$ = 8.0 Hz, 1H), 8.48 (d, $J$ = 5.2 Hz, 1H), 8.65(s, 1H), 9.34(s, 1H), 11.11(s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 117 |    | C | 733.4 | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 1.92-1.94 (m, 1H), 2.02-2.10 (m, 2H), 2.62-2.65 (m, 5H), 3.90 (s, 3H), 4.97-5.02 (m, 2H), 5.10 (s, 2H), 5.37 (t, $J$ = 6 Hz, 1H), 6.85 (d, $J$ = 8.4 Hz, 1H), 7.20-7.22 (m, 1H), 7.34-7.41 (m, 2H), 7.45 (d, $J$ = 2.0 Hz, 1H), 7.50-7.56 (m, 2H), 7.75-7.77 (m, 2H), 8.02-8.06 (m, 2H), 8.21 (d, $J$ = 8.0 Hz, 1H), 8.37 (d, $J$ = 6.0 Hz, 1H), 8.42 (d, $J$ = 2.4 Hz, 1H), 9.18 (s, 1H).                                                                                 |
| 118 |  | C | 856.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.98-2.03 (m, 1H), 2.09-2.15 (m, 1H), 2.20-2.24 (m, 1H), 2.70-2.87 (m, 5H), 4.01-4.04 (m, 4H), 4.29-4.34 (m, 1H), 4.46 (s, 2H), 4.75-4.79 (m, 1H), 4.89-4.95 (m, 1H), 5.00-5.06 (m, 1H), 5.33-5.40 (m, 2H), 5.65-5.70 (m, 1H), 6.53-6.55 (m, 1H), 6.79 (s, 1H), 7.08-7.11 (m, 1H), 7.40 (d, $J$ = 8.0 Hz, 1H), 7.56-7.65 (m, 4H), 7.95 (s, 1H), 8.19-8.30 (m, 3H), 8.60-8.64 (m, 2H), 9.38 (s, 1H).                                                                      |
| 119 |  | C | 990.7 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 0.93 (s, 9H), 1.35 (t, $J$ = 6.8 Hz, 3H), 1.77-1.78 (s, 1H), 2.02-2.04 (m, 1H), 2.44 (s, 3H), 3.53-3.64 (m, 14H), 3.80-3.85 (m, 2H), 3.95 (s, 2H), 4.28 (s, 1H), 4.44 (d, $J$ = 8.2 Hz, 1H), 4.54 (d, $J$ = 9.6 Hz, 1H), 4.58-4.63 (m, 2H), 4.90 (s, 1H), 5.12 (s, 1H), 7.26-7.50 (m, 5H), 7.54 (d, $J$ = 5.8 Hz, 1H), 7.66 (d, $J$ = 8.2 Hz, 1H), 7.90 (s, 1H), 8.35 (d, $J$ = 8.0 Hz, 1H), 8.42-8.45 (m, 3H), 8.85 (s, 1H), 8.97 (s, 1H), 9.41 (s, 1H), 11.92 (s, 1H). |
| 120 |  | C | 790.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 0.95 (s, 9H), 1.37-1.47 (m, 3H), 1.75-1.81 (m, 1H), 2.03-2.08 (m, 1H), 2.44 (s, 3H), 3.16-3.17 (m, 4H), 3.29 (s, 2H), 3.54-3.63 (m, 2H), 3.89 (s, 2H), 4.06 (s, 3H), 4.26-4.31 (m, 1H), 4.44-4.51 (m, 3H), 4.56-4.61 (m, 1H), 4.90-4.96 (m, 1H), 5.10-5.17                                                                                                                                                                                                               |

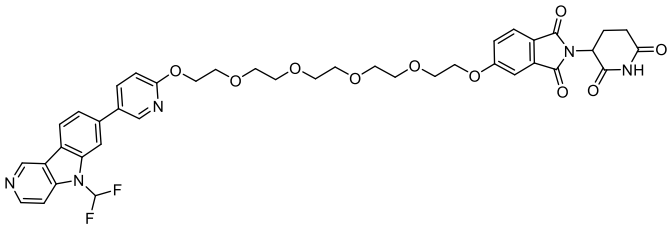
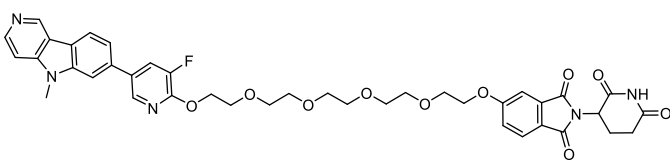
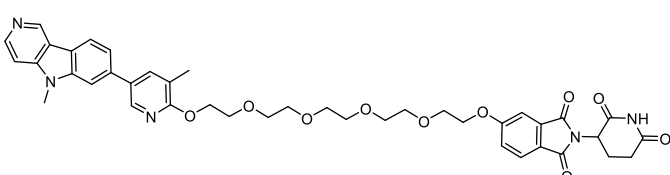
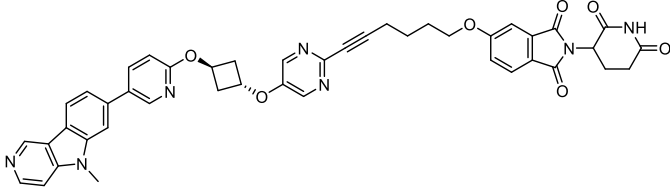
|     |                                                                                     |   |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-----|-------------------------------------------------------------------------------------|---|--------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |        | (m, 1H), 7.06-7.10 (m, 1H), 7.36-7.38 (m, 2H), 7.42-7.48 (m, 3H), 7.53-7.56 (m, 1H), 7.57-7.61 (m, 1H), 7.80 (s, 1H), 8.10-8.14 (m, 1H), 8.32 (s, 1H), 8.44-8.46 (m, 2H), 8.58 (d, $J$ = 2.0 Hz, 1H), 8.97 (s, 1H), 9.40 (s, 1H), 11.90-11.98 (m, 1H).                                                                                                                                                                                                                                                                                                                                                                                        |
| 121 |    | B | 966.7  | <sup>1</sup> H NMR (400 MHz, DMSOd-6): $\delta$ 0.93 (s, 9H), 1.36-1.47 (m, 3H), 1.73-1.80 (m, 1H), 1.96-2.09 (m, 2H), 3.23-3.60 (m, 16H), 3.79 (t, $J$ = 3.6 Hz, 2H), 3.96 (s, 2H), 4.28 (s, 1H), 4.42-4.46 (m, 3H), 4.54 (d, $J$ = 9.6 Hz, 1H), 4.90 (t, $J$ = 7.6 Hz, 1H), 5.12 (s, 1H), 6.97 (d, $J$ = 8.4 Hz, 1H), 7.35-7.43 (m, 5H), 7.65-7.69 (m, 2H), 7.87 (s, 1H), 8.12-8.15 (m, 1H), 8.37-8.43 (m, 2H), 8.51 (d, $J$ = 5.6 Hz, 1H), 8.59 (d, $J$ = 1.6 Hz, 1H), 8.97 (s, 1H), 9.51 (s, 1H), 12.28 (s, 1H).                                                                                                                          |
| 122 |  | C | 1010.7 | <sup>1</sup> H NMR (400 MHz, DMSOd-6): $\delta$ 0.93 (s, 9H), 1.36 (d, $J$ = 7.2 Hz, 3H), 1.73-1.80 (m, 1H), 2.01-2.05 (m, 1H), 2.44 (s, 1H), 3.51-3.60 (m, 20H), 3.78 (t, $J$ = 4.4 Hz, 2H), 3.95 (s, 2H), 4.06-4.10 (m, 1H), 4.27 (s, 1H), 4.42-4.46 (m, 3H), 4.54 (d, $J$ = 9.6 Hz, 1H), 4.90 (t, $J$ = 7.2 Hz, 1H), 5.12 (d, $J$ = 3.6 Hz, 1H), 6.97 (d, $J$ = 8.8 Hz, 1H), 7.35-7.38 (m, 3H), 7.41-7.43 (m, 2H), 7.48 (d, $J$ = 5.6 Hz, 1H), 7.56 (d, $J$ = 8.0 Hz, 1H), 7.77 (s, 1H), 8.10-8.13 (m, 1H), 8.30 (d, $J$ = 8.0 Hz, 1H), 8.42 (d, $J$ = 6.0 Hz, 2H), 8.56 (d, $J$ = 2.4 Hz, 1H), 8.97 (s, 1H), 9.35 (s, 1H), 11.79 (s, 1H). |
| 123 |  | C | 839.6  | <sup>1</sup> HNMR (400 MHz, DMSO- $d_6$ ): $\delta$ : 11.11(s, 1H), 9.39(s,1H), 8.91(s,1H), 8.51(s,1H), 8.36(d, $J$ = 8.0 Hz, 1H), 8.19(s, 1H), 8.10(s,1H), 7.83(d, $J$ = 8.4 Hz, 1H), 7.71(d, $J$ = 8.4 Hz, 1H), 7.64(d, $J$ = 5.2 Hz, 1H), 7.43(s, 1H), 7.34(d, $J$ = 8.0 Hz, 1H), 5.42-5.47(m, 1H), 5.09-5.14(m, 1H), 4.36(s, 1H), 4.18(t, $J$ = 6.4 Hz, 2H), 4.24(t, $J$ = 4.8 Hz, 2H), 3.98(s, 3H), 2.80-2.91(m, 1H), 2.74-2.76(m, 2H), 2.40-                                                                                                                                                                                            |

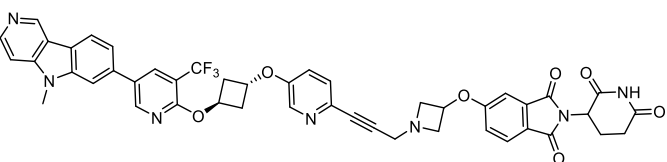
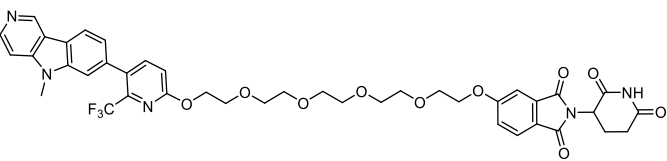
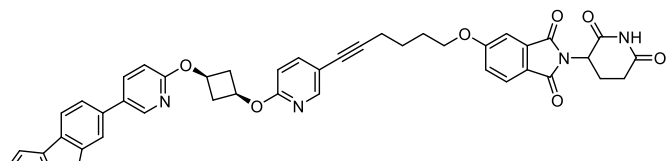
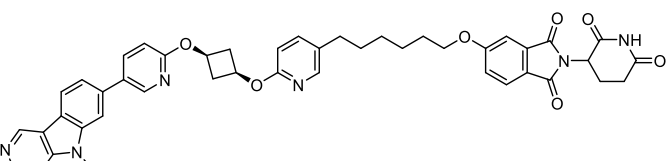
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-----|-------------------------------------------------------------------------------------|---|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | 2.46(m, 4H), 2.32(t, $J$ = 6.4 Hz, 2H), 2.05-2.07(m, 4H), 1.76-1.82(m, 4H), 1.44-1.48(m, 4H).                                                                                                                                                                                                                                                                                                                                                                                                                                |
| 124 |    | C | 774.5 | <sup>1</sup> H NMR(400 MHz, CDCl <sub>3</sub> ):<br>δ 8.49 (s, 1H), 8.22 (m, $J$ = 7.6 Hz, 1H), 8.17 (s, 1H), 7.94 (d, $J$ = 2 Hz, 1H), 7.76 (d, $J$ = 8.4 Hz, 1H), 7.59 (s, 1H), 7.52 (d, $J$ = 7.6 Hz, 1H), 7.34 (d, $J$ = 1.2 Hz, 1H), 7.30-7.27 (m, 4H), 7.20-7.18 (m, 1H), 6.87 (d, $J$ = 8.8 Hz, 1H), 6.74 (d, $J$ = 8.4 Hz, 2H), 5.52-5.54 (m, 1H), 4.97-4.94 (m, 2H), 4.16 (t, $J$ = 6.0 Hz, 2H), 3.92 (s, 3H), 2.88-2.69 (m, 8H), 2.50 (t, $J$ = 6.8 Hz, 2H), 2.16-2.13 (m, 2H), 1.82-1.78 (m, 2H).                 |
| 125 |  | C | 841.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.85-1.90 (m, 4H), 2.08-2.19 (m, 2H), 2.20-2.26 (m, 2H), 2.44-2.57 (m, 4H), 2.70-2.90 (m, 3H), 3.45-3.49 (m, 2H), 3.53-3.56 (m, 6H), 3.88-3.91 (m, 2H), 4.22-4.29 (m, 3H), 4.47-4.48 (m, 1H), 4.90-4.94 (m, 1H), 5.53-5.55 (m, 1H), 6.51 (d, $J$ = 8.0 Hz, 1H), 6.77 (s, 1H), 7.47 (d, $J$ = 17.2 Hz, 2H), 7.58 (s, 1H), 7.60 (d, $J$ = 8.4 Hz, 1H), 8.16 (s, 1H), 8.23-8.28 (m, 2H), 8.60 (s, 2H), 9.41 (s, 1H).                                                      |
| 126 |  | B | 796.6 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.42-1.51 (m, 4H), 1.75-1.79 (m, 2H), 2.03-2.06 (m, 1H), 2.54 (s, 3H), 2.58-2.68 (m, 5H), 2.81-2.94 (m, 2H), 3.11-3.17 (m, 2H), 3.61-3.71 (m, 3H), 3.98-4.11 (m, 6H), 4.15 (s, 3H), 4.17-4.23 (m, 3H), 5.10-5.14 (m, 1H), 5.25-5.31 (m, 1H), 7.03 (d, $J$ = 8.4 Hz, 1H), 7.33-7.42 (m, 2H), 7.84-7.89 (m, 1H), 8.22-8.32 (m, 3H), 8.55 (d, $J$ = 8.0 Hz, 1H), 8.71 (s, 1H), 8.78 (d, $J$ = 6.4 Hz, 1H), 9.78 (s, 1H), 10.05 (brs, 1H), 10.51 (brs, 1H), 11.11 (s, 1H). |
| 127 |  | C | 683.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.11-1.23 (m, 4H), 1.82-1.99 (m, 4H), 2.30-2.39 (m, 3H), 2.60 (br, 4H), 2.86-2.94 (m, 3H), 3.17 (s, 2H), 3.98 (s, 3H), 4.10 (br, 1H), 4.21 (d, $J$ = 16.8 Hz, 1H), 4.32-4.41(m, 3H), 5.05 (dd, $J$ = 13.2 Hz, 1H), 6.96 (d, $J$ =                                                                                                                                                                                                                                      |

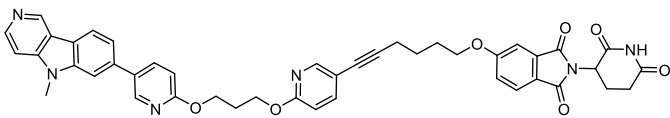
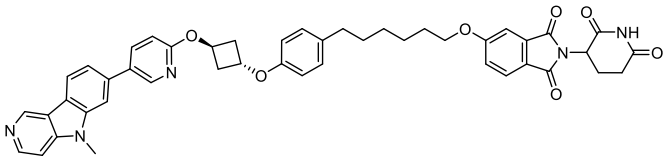
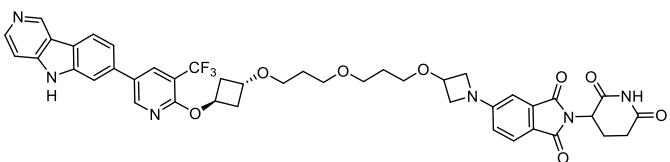
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|-----|-------------------------------------------------------------------------------------|---|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | 9.2 Hz ,1H), 706-7.08 (m, 2H), 7.53 (d, $J$ = 8.4 Hz, 1H), 7.62 (d, $J$ = 8.0 Hz, 1H), 7.69 (d, $J$ = 6.0 Hz,1H),7.95 (s, 1H), 8.02 (dd, $J$ = 9.2 Hz, 1H), 8.30 (dd, $J$ = 8.4 Hz, 1H), 8.51 (d, $J$ = 5.6 Hz, 1H), 8.64 (s, 1H), 9.38 (s, 1H), 10.95 (s, 1H).                                                                                                                                                                                                                                                          |
| 128 |   | C | 697.6 | <sup>1</sup> H NMR (400 MHz, DMSO-d6) δ 1.16-1.23 (m, 3H), 1.40-1.50 (m, 2H), 1.61 (br, 1H), 1.76-1.78 (m, 2H), 1.94-1.96 (m, 1H), 2.38-2.41 (s, 3H), 2.51-2.56 (m, 4H), 2.82-2.90 (m, 3H), 3.29-3.33 (m, 4H), 3.95 (s, 3H), 4.18-4.22 (m, 1H), 4.30-4.39 (m, 3H), 5.02-5.08 (m, 1H), 6.95 (d, $J$ = 8.8 Hz, 1H), 7.05-7.06 (m, 2H), 7.50-7.69 (m, 3H), 7.91 (s, 1H), 8.00 (dd, $J$ = 8.8, 2.2 Hz, 1H), 8.28 (d, $J$ = 8.0 Hz, 1H), 8.48 (d, $J$ = 5.8 Hz, 1H), 8.62 (d, $J$ = 2.0 Hz, 1H), 9.33 (s, 1H), 10.95 (s, 1H). |
| 129 |  | C | 818.5 | <sup>1</sup> HNMR (400 MHz, CDCl <sub>3</sub> ): δ 9.25 (s, 1H), 8.48 (s, 1H), 8.39 (s, 1H), 8.09 (d, $J$ =8.0 Hz, 1H), 7.82 (d, $J$ =8.0 Hz, 1H), 7.72 (d, $J$ =8.4 Hz, 1H), 7.46 (s, 1H), 7.36-7.41 (m, 2H), 7.19-7.24 (m, 2H), 6.82 (d, $J$ =8.8 Hz, 1H), 4.86-4.91 (m, 1H), 4.58-4.63 (m, 1H), 4.45-4.48 (m, 2H), 3.78-3.82 (m, 5H), 3.55-3.80 (m, 9H), 3.39-3.50 (m, 3H), 2.69-2.82 (m, 6H), 1.96-2.05 (m, 2H), 1.81-1.89 (m, 2H).                                                                                  |
| 130 |  | B | 854.6 | <sup>1</sup> H NMR (400 MHz, DMSO-d6): δ 1.74-1.80 (m, 4H), 1.85-1.92 (m, 2H), 1.97-2.02 (m, 2H), 2.02-2.15 (m, 2H), 2.54-2.58 (m, 2H), 2.67-2.91 (m, 4H), 3.41-3.50 (m, 8H), 3.81-3.88 (m, 2H), 3.98 (s, 3H), 4.25 (t, $J$ = 7.8 Hz, 2H), 4.44-4.49 (m, 1H), 5.05 (dd, $J$ = 5.2, 12.8 Hz, 1H), 5.33-5.40 (m, 1H), 6.66 (dd, $J$ = 1.6, 8.4 Hz, 1H), 6.80 (d, $J$ = 1.2 Hz, 1H), 7.63-7.72 (m, 3H), 8.10 (s, 1H), 8.36 (d, $J$ = 8.4Hz, 1H), 8.51 (d, $J$ = 4.8 Hz, 2H), 8.92 (s, 1H), 9.39 (s, 1H), 11.06 (s, 1H).     |

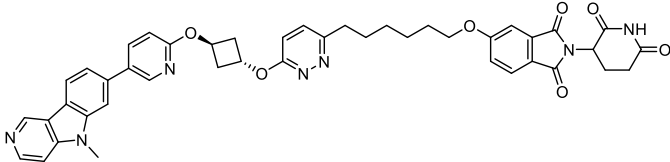
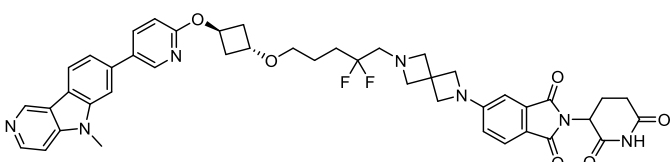
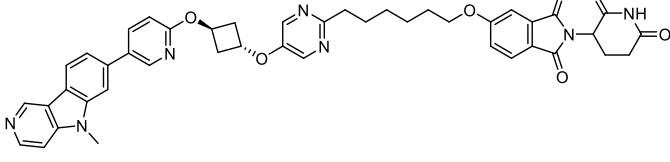
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-----|-------------------------------------------------------------------------------------|---|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 131 |    | A | 796.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.99-2.05 (m, 1H), 2.55-2.67 (m, 3H), 2.84-2.93 (m, 1H), 3.51-3.60 (m, 16H), 3.77 (d, J = 3.6 Hz, 4H), 4.02 (s, 3H), 4.28 (m, 2H), 4.45 (t, J = 3.6 Hz, 2H), 5.09-5.13 (m, 1H), 6.98 (d, J = 8.4 Hz, 1H), 7.32-7.35 (m, 1H), 7.41 (d, J = 0.8 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.78-7.82 (m, 2H), 8.06 (s, 1H), 8.20-8.23 (m, 1H), 8.38 (d, J = 8.4 Hz, 1H), 8.58 (d, J = 6.4 Hz, 1H), 8.66 (d, J = 1.6 Hz, 1H), 8.66 (s, 1H), 9.48 (s, 1H), 11.12 (s, 1H).</p> |
| 132 |  | A | 840.6 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 2.01-2.05 (m, 1H), 2.56-2.67 (m, 2H), 2.84-2.89 (m, 1H), 3.49-3.59 (m, 20H), 3.75-3.79 (m, 4H), 3.96 (s, 3H), 4.27-4.29 (m, 2H), 4.43-4.45 (m, 2H), 5.09-5.13 (m, 1H), 6.96-6.99 (m, 1H), 7.32-7.35 (m, 1H), 7.41-7.42 (m, 1H), 7.62-7.65 (m, 2H), 7.79-7.81 (m, 1H), 7.99 (s, 1H), 8.19-8.21 (m, 1H), 8.31-8.34 (m, 1H), 8.50-8.51 (m, 1H), 8.64-8.65 (m, 1H), 9.37 (s, 1H), 11.11 (s, 1H).</p>                                                                  |
| 133 |  | A | 757.6 | <p><sup>1</sup>H NMR (400 Hz, D<sub>6</sub>-DMSO): δ 1.24-1.35 (m, 7H), 1.46-1.57 (m, 8H), 1.72-1.82 (m, 2H), 1.98-2.01 (m, 3H), 2.57-2.74 (m, 3H), 2.81-2.99 (m, 2H), 3.57-3.59 (m, 2H), 3.98 (s, 3H), 4.06-4.08 (m, 2H), 4.33 (s, 2H), 5.03-5.06 (m, 1H), 6.54-6.66 (m, 1H), 6.69 (s, 1H), 6.93-6.95 (m, 1H), 7.57-7.71 (m, 3H), 8.02 (s, 1H), 8.19-8.21 (m, 1H), 8.34-8.36 (m, 1H), 8.53-8.58 (m, 1H), 8.66 (s, 1H), 9.41 (s, 1H), 11.08 (s, 1H).</p>                                                                |
| 134 |  | B | 776.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.74-1.78 (m, 2H), 1.92-1.95 (m, 2H), 2.03-2.07 (m, 1H), 2.54-2.62 (m, 4H), 2.68-2.71 (m, 4H), 2.85-2.93 (m, 1H), 3.96 (s, 3H), 4.23-4.27 (m, 2H), 5.09-5.14 (m, 1H), 5.45-5.48 (m, 1H), 5.55-5.58 (m, 1H), 7.01 (d, J = 8.8 Hz, 1H), 7.24-7.26 (m, 1H), 7.36-7.38 (m, 1H), 7.45 (m, 1H), 7.62-7.68 (m, 3H), 7.82 (d, J = 8.0 Hz, 1H), 7.99 (s, 1H), 8.21-8.24 (m, 1H),</p>                                                                                       |

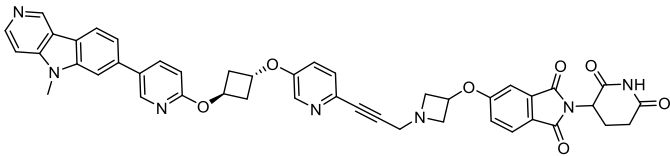
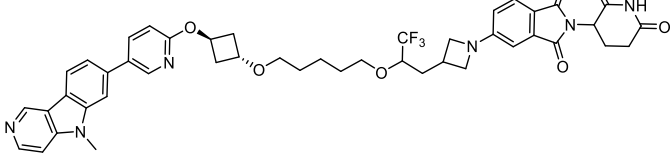
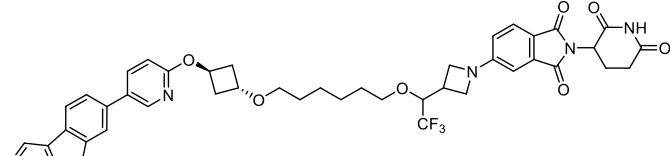
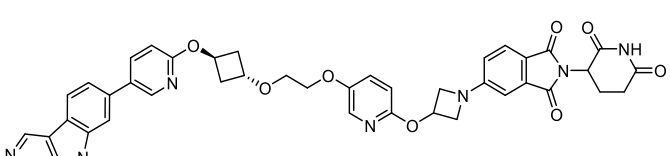
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-----|-------------------------------------------------------------------------------------|---|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | 8.33 (d, $J$ = 8.0 Hz, 1H),<br>8.49-8.51(m, 1H), 8.64-8.65<br>(m, 1H), 9.37(s, 1H), 11.12<br>(s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| 135 |    | B | 783.6 | <sup>1</sup> H NMR (400 MHz, DMSO-<br>d <sub>6</sub> ): 1.60-1.80 (m, 6H), 1.92-<br>2.07 (m, 5H), 2.16-2.26 (m,<br>3H), 2.34-2.40 (m, 2H),<br>2.55-2.67 (m, 4H), 2.84-2.93<br>(m, 1H), 3.26-3.31 (m, 4H),<br>3.78-3.82 (m, 1H), 3.96 (s,<br>3H), 4.18 (t, $J$ = 6.0 Hz, 2H),<br>5.05-5.27 (m, 2H), 6.90-6.94<br>(m, 1H), 7.33-7.35 (m, 1H),<br>7.42 (s, 1H), 7.60-7.63 (m,<br>2H), 7.83 (d, $J$ = 8.4 Hz, 1H),<br>7.98 (s, 1H), 8.17-8.20 (m,<br>1H), 8.32 (d, $J$ = 8.0 Hz, 1H),<br>8.51 (d, $J$ = 6.0 Hz, 1H), 8.62<br>(s, 1H), 9.36 (s, 1H), 11.12<br>(s, 1H).                                                   |
| 136 |  | C | 797.5 | <sup>1</sup> H NMR (400 MHz, DMSO-<br>d <sub>6</sub> ): $\delta$ 1.61-1.65 (m, 2H),<br>1.77-1.80 (m, 2H), 1.99-2.08<br>(m, 4H), 2.14-2.20 (m, 2H),<br>2.44-2.46 (m, 3H), 2.55-2.61<br>(m, 4H), 2.72-2.76 (m, 1H),<br>2.85-2.93 (m, 1H), 3.79-3.84<br>(m, 3H), 3.96 (s, 3H), 4.04-<br>4.09 (m, 2H), 4.17-4.20 (m,<br>2H), 5.10-5.14 (m, 2H), 6.93<br>(d, $J$ = 8.4 Hz, 1H), 7.34-7.42<br>(m, 2H), 7.61-7.65 (m, 2H),<br>7.83 (d, $J$ = 8.0 Hz, 1H), 7.99<br>(s, 1H), 8.18-8.20 (m, 1H),<br>8.32 (d, $J$ = 8.4 Hz, 1H), 8.50<br>(d, $J$ = 6.0 Hz, 1H), 8.62 (d, $J$<br>= 0.8 Hz, 1H), 9.37 (s, 1H),<br>11.12 (s, 1H). |
| 137 |  | C | 810.6 | <sup>1</sup> H NMR (400 MHz, DMSO-<br>d <sub>6</sub> ): $\delta$ 1.58-1.63 (m, 2H),<br>1.72-1.77 (m, 2H), 2.03-2.11<br>(m, 3H), 2.33-2.47 (m, 8H),<br>2.54-2.62 (m, 2H), 2.78-2.90<br>(m, 3H), 3.41-3.48 (m, 3H),<br>3.75-3.79 (m, 1H), 3.80-3.87<br>(m, 1H), 4.02 (s, 3H), 4.06 (s,<br>1H), 4.13-4.18 (m, 3H),<br>5.10-5.14 (m, 1H), 5.25-5.28<br>(m, 1H), 6.96-7.00 (m, 1H),<br>7.33-7.42 (m, 2H), 7.70 (d, $J$<br>= 8.4 Hz, 1H), 7.80-7.84 (m,<br>2H), 8.06 (s, 1H), 8.23-8.26<br>(m, 1H), 8.39 (d, $J$ = 8.0 Hz,<br>1H), 8.57-8.67 (m, 2H), 9.49<br>(s, 1H), 11.12 (s, 1H).                                     |

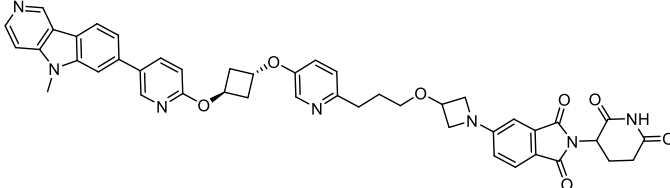
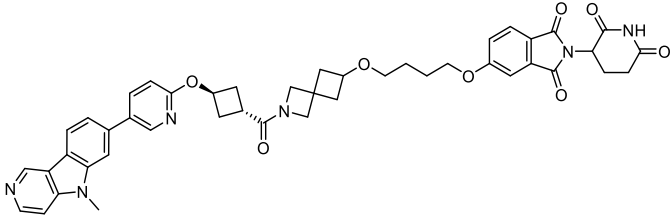
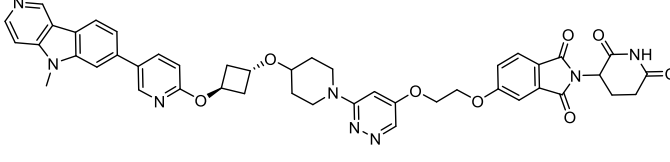
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-----|-------------------------------------------------------------------------------------|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 138 |    | B | 788.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d6): δ 2.01-2.04 (m, 1H), 2.56-2.67 (m, 2H), 2.83-2.93 (m, 1H), 3.52-3.59 (m, 12H), 3.78 (s, 4H), 4.29 (s, 2H), 4.45 (s, 2H), 5.11 (d, <i>J</i> = 12.8 Hz, 1H), 6.98 (d, <i>J</i> = 8.8 Hz, 1H), 7.34 (d, <i>J</i> = 8.4 Hz, 1H), 7.43 (s, 1H), 7.76-7.83(m, 3H), 8.14-8.18 (m, 2H), 8.36-8.50 (m, 2H), 8.61-8.65(m, 2H), 9.49 (s, 1H), 11.11 (s, 1H).                                                                                                                                                                                          |
| 139 |   | B | 770.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d6): δ 2.00-2.03 (m, 1H), 2.59-2.74 (m, 2H), 2.87 (t, <i>J</i> = 11.6 Hz, 1H), 3.52-3.60 (m, 12H), 3.80 (d, <i>J</i> = 19.2 Hz, 4H), 4.03 (s, 3H), 4.28 (s, 2H), 4.54 (s, 2H), 5.11 (d, <i>J</i> = 12.8 Hz, 1H), 7.33 (d, <i>J</i> = 7.6 Hz, 1H), 7.42 (s, 1H), 7.78 (m, 2H), 7.86 (d, <i>J</i> = 4.0 Hz, 1H), 8.13 (s, 1H), 8.27 (d, <i>J</i> = 11.2 Hz, 1H), 8.41 (d, <i>J</i> = 7.6 Hz, 1H), 8.52 (s, 1H), 8.61 (d, <i>J</i> = 4.8 Hz, 1H), 9.53 (s, 1H), 11.11 (s, 1H).                                                                     |
| 140 |  | A | 766.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d6): δ 1.99-2.05 (m, 1H), 2.26 (s, 3H), 2.52-2.60 (m, 2H), 2.89 (s, 1H), 3.48-3.65 (m, 12H), 3.74-3.83 (m, 4H), 4.04 (s, 3H), 4.24-4.31 (m, 2H), 4.44-4.50 (m, 2H), 5.08-5.13 (m, 1H), 7.32-7.34 (m, 1H), 7.41 (d, <i>J</i> = 2.0 Hz, 1H), 7.72 (d, <i>J</i> = 8.4 Hz, 1H), 7.79 (d, <i>J</i> = 8.4 Hz, 1H), 7.87 (d, <i>J</i> = 6.0 Hz, 1H), 8.04-8.10 (m, 2H), 8.40 (d, <i>J</i> = 8.0 Hz, 1H), 8.49 (d, <i>J</i> = 2.4 Hz, 1H), 8.61 (d, <i>J</i> = 6.4 Hz, 1H), 9.52 (s, 1H), 11.11 (s, 1H).                                                |
| 141 |  | C | 776.5 | <sup>1</sup> H NMR (400 Hz, DMSO-d6): δ 1.72-1.78 (m, 2H), 1.91-2.10 (m, 4H), 2.54-2.57 (m, 2H), 2.67-2.72 (m, 3H), 3.30 (s, 3H), 3.97 (s, 3H), 4.25 (t, <i>J</i> = 6.4 Hz, 2H), 5.11-5.18 (m, 2H), 5.41-5.48 (m, 1H), 7.01 (d, <i>J</i> = 8.8 Hz, 1H), 7.36 (dd, <i>J</i> = 8.8, 2.0 Hz, 1H), 7.46 (d, <i>J</i> = 2.0 Hz, 1H), 7.63-7.67 (m, 2H), 7.82 (d, <i>J</i> = 8.0 Hz, 1H), 8.01 (s, 1H), 8.23 (dd, <i>J</i> = 8.8, 2.4 Hz, 1H), 8.35 (d, <i>J</i> = 8.0 Hz, 1H), 8.44 (s, 2H), 8.52 (d, <i>J</i> = 5.6 Hz, 1H), 8.65 (d, <i>J</i> = 2.4 Hz, 1H), 9.39 (s, 1H), 11.12 (s, |

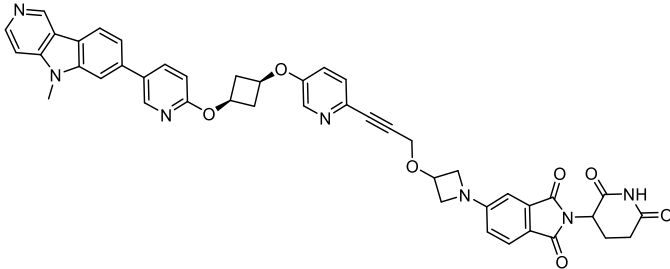
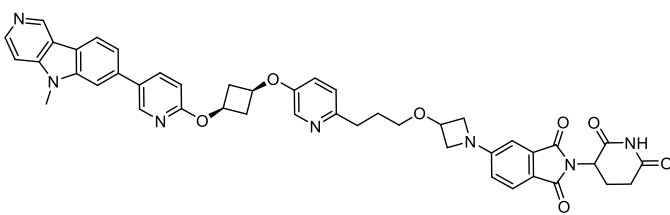
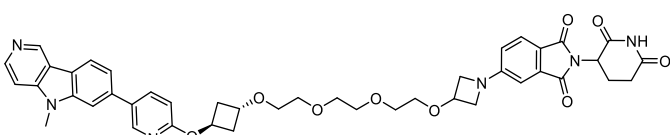
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|-----|-------------------------------------------------------------------------------------|---|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD): δ 1.90-1.94 (m, 2H), 1.99-2.04 (m, 1H), 2.34-2.40 (m, 1H), 2.65-2.70 (m, 4H), 3.46-3.50 (m, 1H), 3.55-3.61 (m, 2H), 3.86-3.90 (m, 1H), 3.96 (s, 3H), 4.89 (m, 2H), 4.95-5.01 (m, 2H), 5.24 (t, <i>J</i> = 4.6Hz, 1H), 5.53-5.59 (m, 1H), 7.12-7.24 (m, 3H), 7.42 (d, <i>J</i> = 5.2 Hz, 1H), 7.60 (d, <i>J</i> = 8.0Hz, 1H), 7.70-7.72 (m, 2H), 7.88 (s, 1H), 8.06 (d, <i>J</i> = 2.8 Hz, 1H), 8.28-8.30 (m, 2H), 8.42 (d, <i>J</i> = 6.4 Hz, 1H), 8.67 (d, <i>J</i> = 2.0 Hz, 1H), 9.29 (s, 1H).                                                                                                                                                  |
| 142 |    | C | 856.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 2.01-2.06 (m, 1H), 2.54-2.68 (m, 2H), 2.84-2.93 (m, 1H), 3.40-3.44 (m, 6H), 3.47-3.51 (m, 4H), 3.56-3.58 (m, 2H), 3.70 (br, 2H), 3.78-3.81 (m, 2H), 3.94 (s, 3H), 4.21 (br, 2H), 4.52 (t, <i>J</i> = 4.0 Hz, 2H), 5.11 (d, <i>J</i> = 12.8 Hz, 1H), 7.26 (d, <i>J</i> = 8.4 Hz, 1H), 7.34 (s, 1H), 7.64 (t, <i>J</i> = 6.8 Hz, 2H), 7.69 (d, <i>J</i> = 6.0 Hz, 1H), 7.74 (d, <i>J</i> = 8.4 Hz, 1H), 8.01 (s, 1H), 8.17 (d, <i>J</i> = 7.6 Hz, 1H), 8.34 (d, <i>J</i> = 8.4 Hz, 1H), 8.53 (d, <i>J</i> = 5.6 Hz, 1H), 9.40 (s, 1H), 11.12 (s, 1H).                                                                                            |
| 143 |  | B | 820.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.68-1.75 (m, 2H), 1.88-1.95 (m, 2H), 2.03-2.08 (m, 1H), 2.16-2.23 (m, 2H), 2.52-2.65 (m, 3H), 2.85-2.93 (m, 1H), 3.08-3.14 (m, 2H), 3.31 (m, 1H), 3.96 (s, 3H), 4.24 (t, <i>J</i> = 6.4 Hz, 2H), 4.94-5.05 (m, 2H), 5.12 (dd, <i>J</i> = 5.2, 12.8 Hz, 1H), 6.81 (d, <i>J</i> = 8.8 Hz, 1H), 6.97 (d, <i>J</i> = 8.8 Hz, 1H), 7.36 (dd, <i>J</i> = 2.0, 8.4 Hz, 1H), 7.44 (d, <i>J</i> = 2.0 Hz, 1H), 7.61-7.70 (m, 3H), 7.82 (d, <i>J</i> = 8.0 Hz, 1H), 7.99 (s, 1H), 8.19-8.21 (m, 2H), 8.32 (d, <i>J</i> = 8.0 Hz, 1H), 8.51 (m, 1H), 8.65 (d, <i>J</i> = 2.0 Hz, 1H), 9.38 (m, 1H), 11.12 (s, 1H).                                       |
| 144 |  | C | 775.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.32-1.38 (m, 2H), 1.42-1.47 (m, 2H), 1.53-1.61 (m, 2H), 1.71-1.78 (m, 2H), 2.01-2.07 (m, 1H), 2.15-2.22 (m, 2H), 2.53-2.61 (m, 4H), 2.84-2.94 (m, 1H), 3.08-3.15 (m, 1H), 3.31 (m, 1H), 3.96 (s, 3H), 4.24 (t, <i>J</i> = 6.4 Hz, 2H), 4.94-5.05 (m, 2H), 5.12 (dd, <i>J</i> = 5.2, 12.8 Hz, 1H), 6.81 (d, <i>J</i> = 8.8 Hz, 1H), 6.97 (d, <i>J</i> = 8.8 Hz, 1H), 7.36 (dd, <i>J</i> = 2.0, 8.4 Hz, 1H), 7.44 (d, <i>J</i> = 2.0 Hz, 1H), 7.61-7.70 (m, 3H), 7.82 (d, <i>J</i> = 8.0 Hz, 1H), 7.99 (s, 1H), 8.19-8.21 (m, 2H), 8.32 (d, <i>J</i> = 8.0 Hz, 1H), 8.51 (m, 1H), 8.65 (d, <i>J</i> = 2.0 Hz, 1H), 9.38 (m, 1H), 11.12 (s, 1H). |
| 145 |  | C | 779.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.32-1.38 (m, 2H), 1.42-1.47 (m, 2H), 1.53-1.61 (m, 2H), 1.71-1.78 (m, 2H), 2.01-2.07 (m, 1H), 2.15-2.22 (m, 2H), 2.53-2.61 (m, 4H), 2.84-2.94 (m, 1H), 3.08-3.15 (m, 1H), 3.31 (m, 1H), 3.96 (s, 3H), 4.24 (t, <i>J</i> = 6.4 Hz, 2H), 4.94-5.05 (m, 2H), 5.12 (dd, <i>J</i> = 5.2, 12.8 Hz, 1H), 6.81 (d, <i>J</i> = 8.8 Hz, 1H), 6.97 (d, <i>J</i> = 8.8 Hz, 1H), 7.36 (dd, <i>J</i> = 2.0, 8.4 Hz, 1H), 7.44 (d, <i>J</i> = 2.0 Hz, 1H), 7.61-7.70 (m, 3H), 7.82 (d, <i>J</i> = 8.0 Hz, 1H), 7.99 (s, 1H), 8.19-8.21 (m, 2H), 8.32 (d, <i>J</i> = 8.0 Hz, 1H), 8.51 (m, 1H), 8.65 (d, <i>J</i> = 2.0 Hz, 1H), 9.38 (m, 1H), 11.12 (s, 1H). |

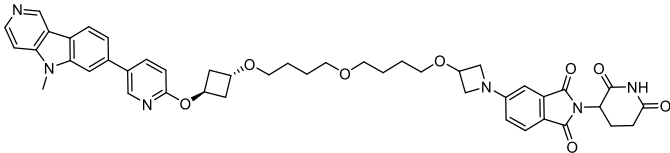
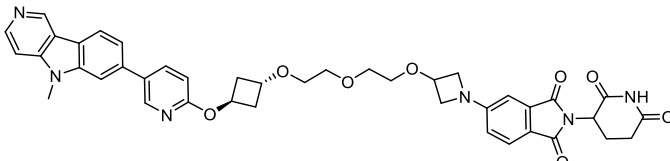
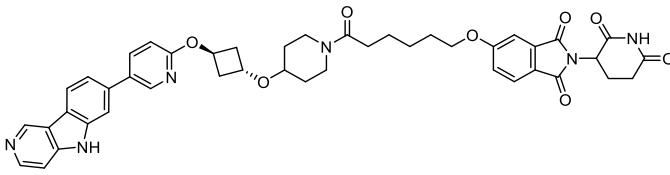
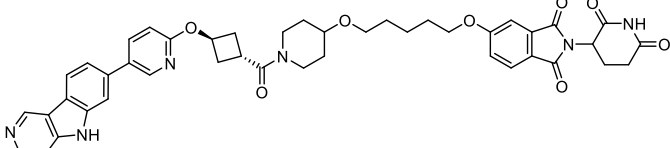
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-----|-------------------------------------------------------------------------------------|---|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | (m, 2H), 4.14-4.17 (m, 5H), 4.91-5.06 (m, 2H), 5.12 (dd, $J = 5.6, 12.8$ Hz, 1H), 6.78 (d, $J = 8.4$ Hz, 1H), 7.01 (d, $J = 8.4$ Hz, 1H), 7.33 (dd, $J = 2.0, 8.4$ Hz, 1H), 7.41 (d, $J = 2.0$ Hz, 1H), 7.61 (dd, $J = 2.0, 8.4$ Hz, 1H), 7.81-7.88 (m, 2H ), 8.00 (d, $J = 2.0$ Hz, 1H), 8.20-8.28 (m, 3H), 8.56 (d, $J = 8.4$ Hz, 1H), 8.71-8.76 (m, 2H), 9.80 (s, 1H),11.12 (s, 1H).                                                                                                                                                                       |
| 146 |   | C | 763.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.67-1.75 (m, 2H), 1.87-1.97 (m, 2H), 2.03-2.07(m, 1H), 2.20-2.23(m, 2H), 2.53-2.67 (m, 4H), 2.85-2.94 (m, 1H), 3.98 (s, 3H), 4.23 (t, $J = 6.0$ Hz, 2H), 4.42-4.49 (m, 4H), 5.10-5.14 (m, 1H), 6.80 (d, $J = 8.4$ Hz, 1H), 6.96 (d, $J = 5.2$ Hz, 1H), 7.34-7.36 (m, 1H), 7.40 (d, $J = 2.0$ Hz, 1H), 7.63-7.69 (m, 3H), 7.82 (d, $J = 8.4$ Hz, 1H), 8.00 (s, 1H), 8.19-8.21 (m, 2H), 8.34 (d, $J = 8.0$ Hz, 1H), 8.51 (d, $J = 6.0$ Hz, 1H), 8.64 (d, $J = 2.4$ Hz, 1H), 9.40 (s, 1H), 11.12 (s, 1H). |
| 147 |  | C | 778.5 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ: 9.32(s, 1H), 8.58(d, $J = 5.6$ Hz, 1H), 8.49(s, 1H), 8.21(d, $J = 8.0$ Hz, 1H), 8.01(s, 1H), 7.92(d, $J = 7.6$ Hz, 1H), 7.77(d, $J = 8.0$ Hz, 1H), 7.56(s, 1H), 7.50(d, $J = 8.0$ Hz, 1H), 7.32(s, 2H), 7.17(d, $J = 8.8$ Hz, 1H), 7.08(d, $J = 8.4$ Hz, 2H), 6.86(d, $J = 8.4$ Hz, 1H), 6.75(d, $J = 7.6$ Hz, 2H), 5.49(s, 1H), 4.94(s, 2H), 4.07(t, $J = 6.4$ Hz, 2H), 3.91(s, 3H), 2.68-2.88(m, 8H), 2.57(t, $J = 6.8$ Hz, 2H), 2.01(s, 2H), 1.83(t, $J = 6.8$ Hz, 3H), 1.62-1.65(m, 2H).             |
| 148 |  | B | 827.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.73-1.79 (m, 4H), 1.95-2.01 (m, 2H), 1.99-2.04 (m, 2H), 2.33-2.39 (m, 2H), 2.44-2.46 (m, 2H), 2.54-2.67 (m, 1H), 2.82-2.91 (m, 1H), 3.37-3.49 (m, 8H), 3.81-3.84 (m, 2H), 4.17-4.25(m, 3H), 4.43-4.48 (m, 1H), 5.01-5.06 (m, 1H), 5.45-5.50 (m, 1H), 6.61-6.64 (m, 1H), 6.77 (d, $J = 4.8$ Hz, 1H), 7.60 (d, $J = 8.4$ Hz, 1H), 7.73 (d, $J = 6.8$ Hz, 1H), 7.97 (s, 1H), 8.471-                                                                                                                       |

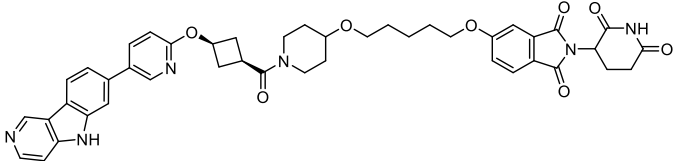
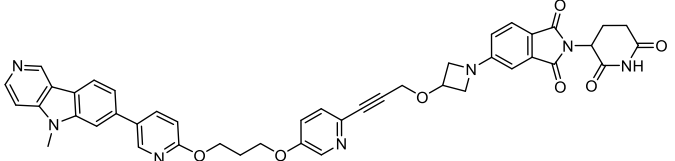
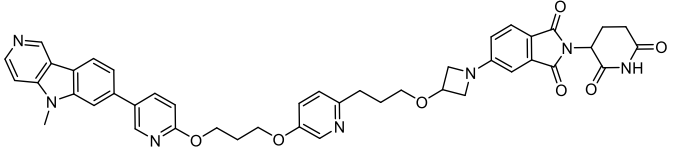
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|-----|-------------------------------------------------------------------------------------|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | 8.43 (m, 2H), 8.54 (d, $J$ = 6.4 Hz, 1H), 8.85 (d, $J$ =4.8 Hz, 1H), 9.55 (s, 1H), 11.06 (s, 1H), 12.44 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 149 |    | B | 780.5 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 1.36-1.49 (m, 4H), 1.66-1.77 (m, 4H), 2.02-2.06 (m, 1H), 2.54-2.68 (m, 6H), 2.81-2.94 (m, 3H), 3.16-3.17 (m, 1H), 3.99 (s, 3H), 4.15-4.18 (m, 2H), 5.09-5.14 (m, 1H), 5.44-5.53 (m, 1H), 7.02 (d, $J$ = 8.8 Hz, 1H), 7.16-7.18 (m, 1H), 7.33-7.35 (m, 1H), 7.45 (m, 1H), 7.54-7.56 (m, 1H), 7.65-7.67 (m, 1H), 7.72-7.73 (m, 1H), 7.81-7.83 (d, $J$ = 8.0 Hz, 1H), 8.03 (s, 1H), 8.22-8.24 (m, 1H), 8.35-8.37 (d, $J$ = 8.0 Hz, 1H), 8.52-8.57 (m, 1H), 8.64-8.65 (m, 1H), 9.42 (s, 1H), 11.11 (s, 1H). |
| 150 |  | B | 804.5 | <sup>1</sup> H NMR: (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ: 10.95 (s, 1H), 9.14 (br s, 1H), 8.15 (s, 1H), 7.52 (d, $J$ = 9.0 Hz, 1H), 7.18 - 7.04 (m, 5H), 6.83 (d, $J$ = 6.7 Hz, 2H), 6.65 (d, $J$ = 8.5 Hz, 1H), 6.61 (s, 1H), 6.54 - 6.47 (m, 3H), 6.26 (d, $J$ = 8.5 Hz, 2H), 5.05 (dd, $J$ = 5.0, 13.3 Hz, 1H), 4.38 - 4.26 (m, 1H), 4.24 - 4.11 (m, 1H), 3.78 (br t, $J$ = 6.5 Hz, 4H), 3.54 - 3.31 (m, 3H), 3.03 - 2.83 (m, 8H), 2.62 - 2.52 (m, 3H), 2.47 - 2.31 (m, 1H), 2.21 - 2.04 (m, 3H), 2.01 - 1.87 (m, 3H), 1.71 (br d, $J$ = 10.7 Hz, 2H).        |
| 151 |  | B | 780.5 | <sup>1</sup> H NMR (400 Hz, DMSO- <i>d</i> <sub>6</sub> ): δ 1.21-1.26 (m, 1H), 1.33-1.48 (m, 4H), 1.69-1.73 (m, 4H), 1.01-2.07 (m, 1H), 2.57-2.68 (m, 5H), 2.79-2.93 (m, 3H), 4.02 (s, 3H), 4.16 (t, $J$ = 6.4 Hz, 2H), 5.09-5.13 (m, 2H), 5.41-5.48 (m, 1H), 7.01 (d, $J$ = 8.8 Hz, 1H), 7.35 (dd, $J$ = 8.4, 1.6 Hz, 1H), 7.46 (d, $J$ = 0.8 Hz, 1H), 7.69 (d, $J$ = 8.0 Hz, 1H), 7.79-7.83 (m, 2H), 8.07 (s, 1H), 8.23 (dd, $J$ = 8.4, 1.2 Hz, 1H), 8.37-8.45 (m, 3H), 8.58 (d, $J$ = 6.0 Hz, 1H), 8.67 (s, 1H), 9.49 (s, 1H), 11.11 (s, 1H),.                    |

|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-----|-------------------------------------------------------------------------------------|---|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 152 |    | A | 788.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 2.01-2.06 (m, 1H), 2.53-2.73 (m, 6H), 2.84-2.92 (m, 1H), 3.59 (s, 2H), 3.81 (t, <i>J</i> = 6.8 Hz, 2H), 3.96 (s, 3H), 5.07-5.14 (m, 3H), 5.42-5.47 (m, 1H), 6.99 (d, <i>J</i> = 8.4 Hz, 1H), 7.28-7.33 (m, 3H), 7.48 (d, <i>J</i> = 8.4Hz, 1H), 7.62-7.65 (m, 2H), 7.84 (d, <i>J</i> = 8.0 Hz, 1H), 7.99 (s, 1H), 8.20-8.24 (m, 2H), 8.33 (d, <i>J</i> = 8.0 Hz, 1H), 8.51 (m, 1H), 8.65 (d, <i>J</i> = 2.4 Hz, 1H), 9.38 (m, 1H), 11.11 (s, 1H).                                                                                                      |
| 153 |  | B | 839.6 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.38-1.41 (m, 2H), 1.54-1.59 (m, 4H), 1.92-1.96 (m, 3H), 2.23-2.45 (m, 5H), 2.82-3.02 (m, 2H), 3.34 (t, <i>J</i> = 6.0 Hz, 2H), 3.56-3.62 (m, 1H), 3.67-3.79 (m, 3H), 4.04-4.05 (m, 1H), 4.14-4.21 (m, 6H), 5.01-5.06 (m, 1H), 5.29-5.35 (m, 1H), 6.61 (d, <i>J</i> = 8.0 Hz, 1H), 6.74 (s, 1H), 6.96 (d, <i>J</i> = 8.4 Hz, 1H), 7.61 (d, <i>J</i> = 8.0 Hz, 1H), 7.86 (d, <i>J</i> = 8.0 Hz, 1H), 8.21-8.25 (m, 3H), 8.53 (d, <i>J</i> = 8.4 Hz, 1H), 8.68 (d, <i>J</i> = 1.6 Hz, 1H), 8.77 (d, <i>J</i> = 6.8 Hz, 1H), 9.77 (s, 1H), 11.07 (s, 1H). |
| 154 |  | C | 839.6 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.26 (s, 4H), 1.36-1.37 (m, 2H), 1.49-1.54 (m, 2H), 1.97-2.00 (m, 1H), 2.29-2.42 (m, 4H), 2.53-2.59 (m, 2H), 2.83-2.91 (m, 1H), 3.17-3.23 (m, 3H), 3.65-3.71 (m, 1H), 3.78-3.89 (m, 2H), 3.96 (s, 3H), 3.98-4.02 (m, 1H), 4.11-4.22 (m, 3H), 4.33-4.36 (m, 1H), 5.04-5.08 (m, 1H), 5.28-5.34 (m, 1H), 6.68-6.70 (m, 1H), 6.83-6.84 (m, 1H), 6.93-6.95 (m, 1H), 7.61-7.66 (m, 3H), 7.98 (s, 1H), 8.17-8.20 (m, 1H), 8.31-8.33 (m, 1H), 8.49-8.51 (m, 1H), 8.63-8.64 (m, 1H), 9.36 (s, 1H), 11.07 (s, 1H).                                               |
| 155 |  | C | 794.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 2.33-2.50 (m,6H), 2.54-2.60 (m, 1H), 2.83-2.93 (m, 1H), 3.68 (t, <i>J</i> = 4.4 Hz, 2H), 3.96 (s, 3H), 4.01 (d, <i>J</i> = 3.6 Hz, 2H), 4.15 (t, <i>J</i> = 4.0 Hz, 2H), 4.28-4.33(m, 1H), 4.45-4.49 (m,2H), 4.04 (s, 1H), 5.06 (d,                                                                                                                                                                                                                                                                                                                    |

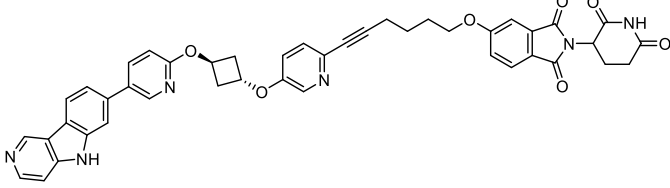
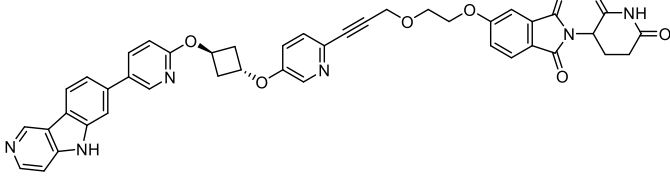
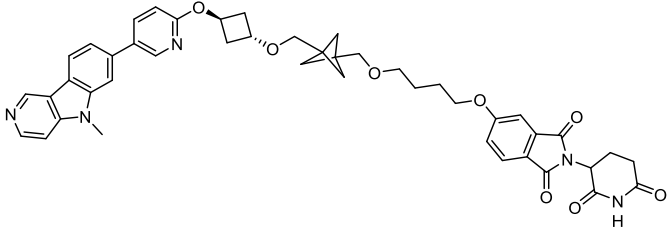
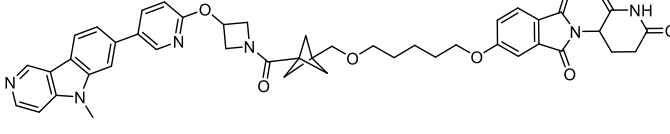
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-----|-------------------------------------------------------------------------------------|---|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | J = 5.2 Hz,1H), 5.31-5.36 (m ,1H), 5.43-5.48 (m,1H), 6.71(dd, J = 2.0 Hz,1H),6.88 (t, J = 9.2 Hz,2H), 6.95 (d, J = 8.8 Hz,1H), 7.50 (d, J = 3.2 Hz, 1H), 7.61-7.65 (m, 1H), 7.91 (d, J = 2.8 Hz,1H), 7.99 (s,1H), 8.18-8.20 (m ,1H), 8.33 (d, J = 8.0 Hz ,1H), 8.50 (d, J = 6.0 Hz, 1H), 8.65 (d, J = 2.4 Hz,1H), 9.37 (s, 1H), 11.08 (s, 1H).                                                                                                                                                                                                                                                               |
| 156 |   | C | 792.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.93-2.01 (m, 3H), 2.54-2.70 (m, 6H), 2.85 (t, J = 7.2 Hz, 2H), 3.45 (t, J = 6 Hz, 2H), 3.79-3.81 (m, 2H), 4.15 (s, 3H), 4.22-4.26 (m, 2H), 4.43-4.45 (m, 1H), 5.03-5.10 (m, 3H), 5.43-5.46 (m, 1H), 6.67 (d, J = 8.4 Hz, 1H), 6.81 (s, 1H), 7.04 (d, J = 8.4 Hz, 1H), 7.46-7.56 (m, 2H), 7.65(d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H), 8.21-8.30 (m, 4H), 8.55 (d, J = 8 Hz,1H), 8.71-8.79 (m, 2H), 9.77 (s, 1H), 11.07 (s, 1H).                                                                                                                 |
| 157 |  | C | 797.5 | <sup>1</sup> HNMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.61-1.66 (m, 2H), 1.75-1.82 (m, 2H), 1.99-2.06 (m, 4H), 2.29-2.33 (m, 2H), 2.43-2.45 (m, 3H), 2.55-2.61(m, 3H), 2.56-2.93 (m, 1H), 3.06-3.09 (m, 1H), 3.31 (s, 1H), 3.80-3.88 (m, 3H), 3.96 (s, 3H), 4.00-4.06 (m, 2H), 4.18 (t, J = 7.4 Hz, 2H), 5.10-5.14 (m, 1H), 5.28-5.33 (m, 1H), 6.93 (d, J = 8.8 Hz, 1H), 7.33-7.36 (m, 1H), 7.42 (d, J = 1.6 Hz, 1H), 7.61-7.64 (m, 2H), 7.83 (d, J = 8.4 Hz, 1H), 7.98 (s, 1H), 8.18-8.20 (m, 1H), 8.32 (d, J = 8.0 Hz, 1H), 8.50 (d, J = 5.6 Hz, 1H), 8.63 (d, J = 2.0 Hz, 1H), 9.37 (s, 1H), 11.12 (s, 1H) |
| 158 |  | C | 823.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.45-1.47 (m , 2H), 1.89-1.92 (m, 2H), 1.97-2.07 (m, 3H), 2.40-2.44 (m, 4H), 2.55-2.67 (m, 1H), 2.84-2.94 (m, 1H), 3.16-3.25 (m, 2H), 3.56-3.64 (m, 1H), 4.05 (s, 3H), 4.10-4.13 (m, 2H),4.42-4.45 (m, 1H), 4.51-4.58 (m, 3H), 5.10-5.15 (m, 1H), 5.31-5.35 (m, 1H),6.78 (s, 1H), 6.97 (d, J = 8.8 Hz, 1H), 7.40-7.42 (m, 1H), 7.51                                                                                                                                                                                                                    |

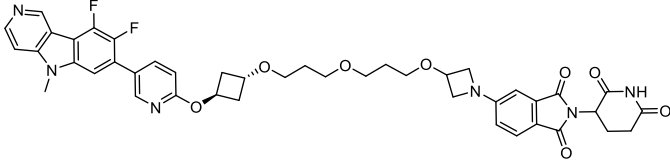
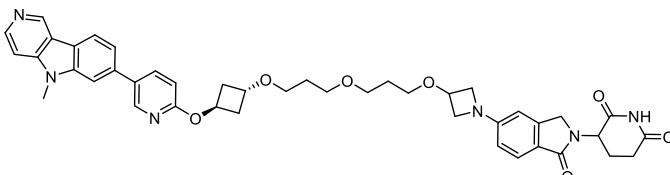
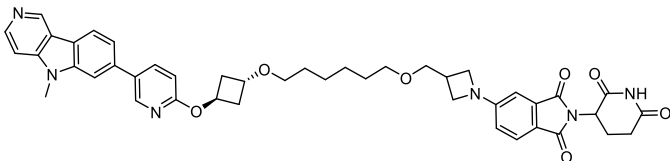
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|-----|-------------------------------------------------------------------------------------|---|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | (s, 1H), 7.85-7.89 (m, 2H), 8.10 (s, 1H), 8.21-8.24 (m, 1H), 8.35 (d, J = 1.6 Hz, 1H), 8.42 (d, J = 8.4 Hz, 1H), 8.62 (d, J = 6.0 Hz, 1H), 8.67 (d, J = 2.4 Hz, 1H), 9.54 (s, 1H), 11.12 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 159 |    | C | 788.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.99-2.03 (m, 2H), 2.21-2.24 (m, 2H), 2.54-2.67 (m, 2H), 2.83-2.92 (m, 1H), 3.16-3.27 (m, 2H), 3.95-3.98 (m, 4H), 3.30-3.34 (m, 2H), 4.49 (s, 2H), 4.66-4.72 (m, 2H), 5.01-5.08 (m, 2H), 6.68 (d, J = 8.4 Hz, 1H), 6.82 (s, 1H), 6.98 (d, J = 8.4 Hz, 1H), 7.37 (dd, J = 8.4 Hz, 1H), 7.54 (d, J = 8.8 Hz, 1H), 7.62-7.67 (m, 3H), 7.99 (s, 1H), 8.21 (d, J = 8.4 Hz, 1H), 8.26 (d, J = 2.8 Hz, 1H), 8.33 (d, J = 8.4 Hz, 1H), 8.50 (d, J = 5.6 Hz, 1H), 8.65 (d, J = 2.0 Hz, 1H), 9.37 (s, 1H), 11.07 (s, 1H).</p>                                                                                   |
| 160 |  | B | 792.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.88-1.95 (m, 2H), 1.97-2.03 (m, 2H), 2.16-2.23 (m, 2H), 2.54-2.60 (m, 1H), 2.67-2.76 (m, 2H), 2.83-2.92 (m, 1H), 3.14-3.21 (m, 2H), 3.43 (t, J = 6.4 Hz, 2H), 3.84 (d, J = 8.8 Hz, 2H), 3.97 (s, 3H), 4.23-4.27 (m, 2H), 4.43-4.48 (m, 1H), 4.56-4.63 (m, 1H), 5.00-5.08 (m, 2H), 6.66 (d, J = 8.0 Hz, 1H), 6.81 (s, 1H), 6.98 (d, J = 8.8 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 7.24-7.27 (m, 1H), 7.62-7.66 (m, 3H), 8.00 (s, 1H), 8.16 (d, J = 2.8 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 8.33 (d, J = 8.0 Hz, 1H), 8.51 (d, J = 5.6 Hz, 1H), 8.65 (d, J = 2.4 Hz, 1H), 9.38 (s, 1H), 11.07 (s, 1H).</p> |
| 161 |  | C | 789.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 2.30-2.36 (m, 2H), 2.40-2.46 (m, 3H), 2.54-2.58 (m, 2H), 2.82-2.91 (m, 1H), 3.44-3.47 (m, 2H), 3.54-3.57 (m, 10H), 3.85 (d, J = 9.2 Hz, 2H), 3.95 (s, 3H), 4.20-4.25 (m, 3H), 4.48-4.50 (m, 1H), 5.04 (t, J = 12.8 Hz, 1H), 5.28-5.33 (m, 1H), 6.62 (d, J = 8.4 Hz, 1H), 6.77 (d, J = 2.0 Hz, 1H), 6.93 (d, J = 8.8 Hz, 1H), 7.60-7.62 (m, 3H), 7.97 (s, 1H), 8.17-8.20 (m,</p>                                                                                                                                                                                                                       |

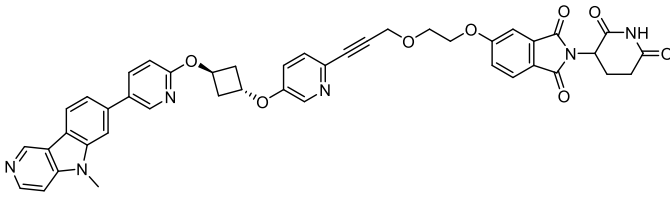
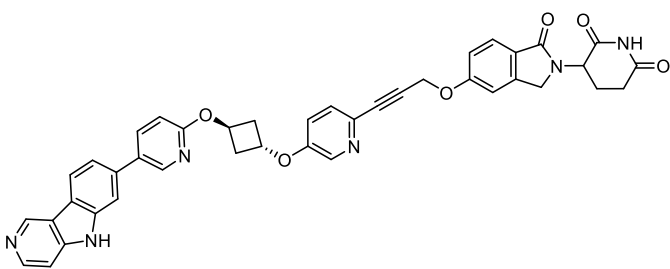
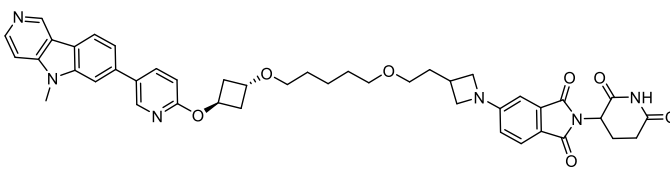
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|-----|-------------------------------------------------------------------------------------|---|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | 1H), 8.49 (d, J = 6.0 Hz,1H),<br>8.63 (d, J = 2.4 Hz, 1H), 9.36<br>(s, 1H), 11.07 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 162 |    | A | 801.6 | 1H NMR (400 MHz, DMSO-d6): δ 1.56 (s, 8H), 1.98-2.01 (m, 1H), 2.34-2.46 (m, 6H), 2.59-2.67 (m, 2H), 2.83-2.92 (m, 1H), 3.38-3.42 (m, 6H), 3.83 (d, J = 5.6 Hz, 2H), 3.96 (s, 3H), 4.18-4.25 (m, 3H), 4.44 (s, 1H), 5.03-5.07 (m, 1H), 5.29-5.33 (m, 1H), 6.63 (d, J = 7.6 Hz, 1H), 6.78 (s, 1H), 6.93 (d, J = 8.8 Hz, 1H), 7.61-7.63 (m, 3H), 7.98 (s, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.31 (d, J = 8.0 Hz, 1H), 8.49 (d, J = 5.6 Hz, 1H), 8.64 (s, 1H), 9.36 (s, 1H), 11.07 (s, 1H).                                                                                             |
| 163 |  | C | 745.5 | 1H NMR (400 MHz, DMSO-d6): δ 1.94-2.00 (m, 1H), 2.31-2.48 (m, 4H), 3.97 (s, 3H), 2.57 (s, 2H), 2.81-2.89 (m, 1H), 3.47-3.49 (m, 2H), 3.54-3.64 (m, 6H), 3.84-3.89 (m, 2H), 4.21-4.29 (m, 3H), 4.52 (s, 1H), 5.02-5.06 (m, 1H), 5.29-5.35 (s, 1H), 6.63-6.66 (m, 1H), 6.79 (d, J = 2.0 Hz, 1H), 6.93 (d, J = 8.8 Hz, 1H), 7.59-7.66 (m, 2H), 7.69 (d, J = 6.0 Hz, 1H), 7.99 (s, 1H), 8.17-8.20 (m, 1H), 8.34 (d, J = 8.0 Hz, 1H), 8.53 (d, J = 6.0 Hz, 1H), 8.62 (d, J = 2.4 Hz, 1H), 9.40 (s, 1H), 11.07 (s, 1H).                                                                |
| 164 |  | C | 785.5 | <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> ): δ 1.52-1.57 (m, 3H), 1.61-1.65 (m, 2H), 1.70-1.74 (m, 2H), 1.98-2.01 (m, 2H), 2.13-2.17 (m, 1H), 2.34-2.41 (m, 2H), 2.47-2.50 (m, 2H), 2.78-2.88 (m, 2H), 3.20-3.28 (m, 2H), 3.54-3.72 (m, 3H), 4.00-4.10 (m, 3H), 4.39-4.44 (m, 1H), 4.95 (dd, J = 5.2, 12.0 Hz, 1H), 5.31-5.42 (m, 4H), 6.82 (d, J = 8.4 Hz, 1H), 7.17 (d, J = 8.8 Hz, 1H), 7.31-7.34 (m, 2H), 7.48-7.51 (m, 2H), 7.68 (s, 1H), 7.77 (d, J = 8.8 Hz, 1H), 7.87 (d, J = 7.2 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 8.32 (s, 1H), 8.41-8.45 (m, 2H), 9.23 (s, 1H). |
| 165 |  | C | 785.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d6): δ 1.35-1.38 (m, 2H), 1.47-1.57 (m, 4H), 1.74-1.81 (m, 4H), 1.99-2.07 (m, 2H), 2.32-2.39 (m, 2H), 2.57 (s,                                                                                                                                                                                                                                                                                                                                                                                                                                 |

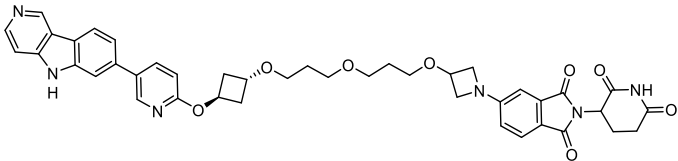
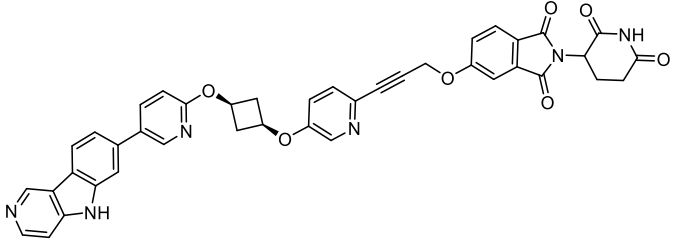
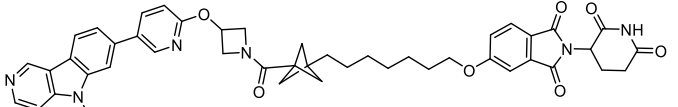
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-----|-------------------------------------------------------------------------------------|---|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | 1H), 2.62-2.67 (m, 2H), 2.82-2.91 (m, 1H), 3.12-3.18 (m, 3H), 3.41-3.51 (m, 4H), 3.85-3.89 (m, 1H), 4.17-4.20 (m, 2H), 5.09-5.14 (m, 1H), 5.18-5.22 (m, 1H), 6.92 (d, J = 8.4 Hz, 1H), 7.33-7.36 (m, 1H), 7.42 (d, J = 1.6 Hz, 1H), 7.47 (d, J = 5.6 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.76 (s, 1H), 7.82 (d, J = 8.4 Hz, 1H), 8.10-8.12 (m, 1H), 8.29 (d, J = 8.0 Hz, 1H), 8.42 (d, J = 6.0 Hz, 1H), 8.54 (d, J = 2.4 Hz, 1H), 9.35 (s, 1H), 11.11 (s, 1H), 11.81 (s, 1H).                                                                                                                                      |
| 166 |  | C | 785.5 | 1H NMR (400 MHz, DMSO-d6): δ 1.31-1.37 (m, 2H), 1.48-1.50 (m, 2H), 1.55-1.57 (m, 2H), 1.76-1.79 (m, 4H), 2.03-2.06 (m, 1H), 2.18-2.27 (m, 2H), 2.55-2.70 (m, 3H), 2.85-2.92 (m, 1H), 3.06-3.17 (m, 4H), 3.42-3.48 (m, 3H), 3.57-3.60 (m, 1H), 3.79-3.83 (m, 1H), 4.17 (t, J = 5.2 Hz, 2H), 5.11-5.15 (m, 2H), 6.91 (d, J = 8.8 Hz, 1H), 7.33-7.36 (m, 1H), 7.42 (s, 1H), 7.48 (d, J = 5.6 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.77 (s, 1H), 7.82 (d, J = 8.0 Hz, 1H), 8.09-8.12 (m, 1H), 8.29 (d, J = 8.0 Hz, 1H), 8.42 (d, J = 5.6 Hz, 1H), 8.53 (d, J = 2.0 Hz, 1H), 9.35 (s, 1H), 11.10 (s, 1H), 11.86 (s, 1H). |
| 167 |  | C | 776.5 | 1HNMR (400 MHz, DMSO-d6): δ 1.99-2.03 m, 2H 2.23-2.27 (m, 2H), 2.56-2.60 (m, 2H), 2.81-2.94 (m, 1H), 3.92-3.94 (m, 1H), 3.96 (s, 3H), 4.24-4.32 (m, 4H), 4.48-4.52 (m, 4H), 4.65-4.72 (m, 1H), 5.03-5.08 (m, 1H), 6.65-6.67 (m, 1H), 6.80-6.81 (m, 1H), 6.97 (t, J = 8.0 Hz, 1H), 7.45-7.46 (m, 1H), 7.53-7.55 (m, 1H), 7.61-7.66 (m, 3H), 7.97 (s, 3H), 8.16-8.21 (m, 1H), 8.31-8.34 (m, 2H), 8.49-8.50 (m, 1H), 8.63-8.64 (m, 1H), 9.36 (s, 1H), 11.07 (s, 1H).                                                                                                                                                 |
| 168 |  | B | 780.5 | 1HNMR (400 MHz, DMSO-d6): δ 1.86-1.93 (m, 2H), 1.91-2.04 (m, 2H), 2.19-2.27 (m, 2H), 2.69-2.77 (m, 2H), 2.81-2.94 (m, 2H), 3.39-3.46 (m, 2H), 3.81-3.84 (m, 2H), 3.96 (s, 3H), 4.14-4.28 (m, 4H), 4.41-4.54 (m, 3H),                                                                                                                                                                                                                                                                                                                                                                                              |

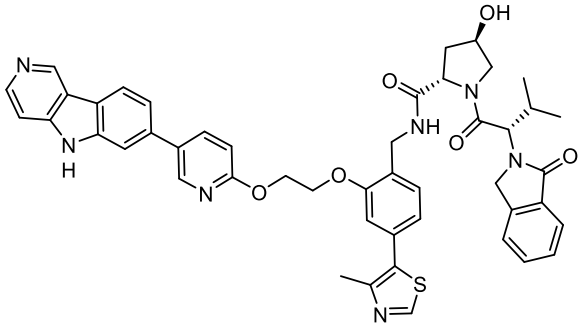
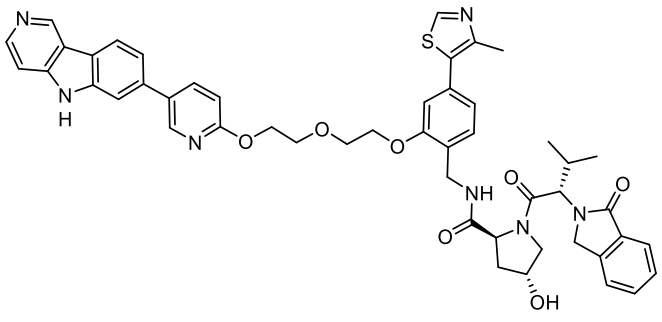
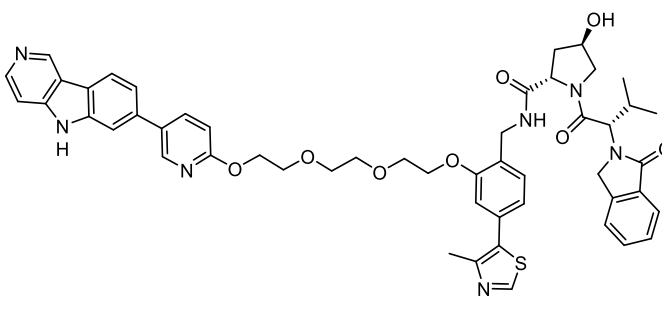


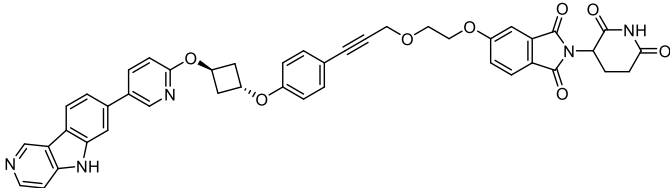
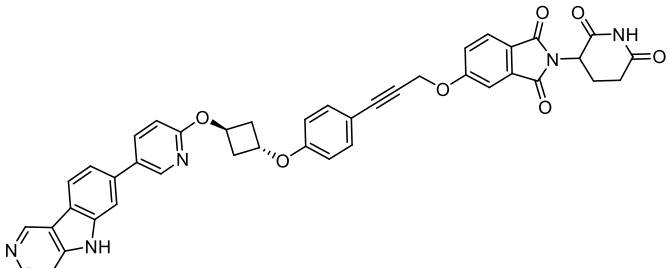
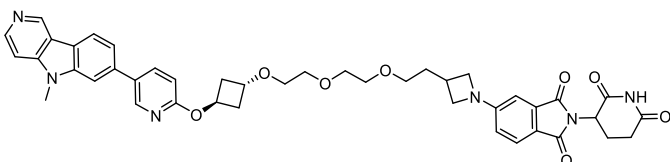
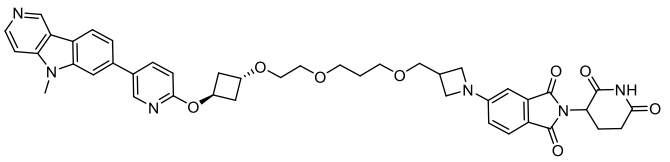
|     |                                                                                     |    |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-----|-------------------------------------------------------------------------------------|----|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |    |       | 2.77 (m, 2H), 2.73 (m, 4H),<br>2.53-2.52 (m, 1H), 2.39-2.38<br>(m, 4H), 1.91 - 1.90 (m, 4H),<br>1.75 (m, 2H), 1.43 ( m, 2H),<br>1.41 (m, 2H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 172 |    | C  | 761.5 | <sup>1</sup> H NMR (400 MHz, DMSO-<br>d6): δ 1.68-1.77 (m, 2H),<br>1.89-1.96 (m, 2H), 2.02-2.08<br>(m, 1H), 2.53-2.69 (m, 8H),<br>2.85-2.94 (m, 1H), 4.25 (t, J<br>= 6.2 Hz, 2H), 5.05-5.14 (m,<br>2H), 5.41-5.47 (m, 1H), 7.01<br>(d, J = 8.4 Hz, 1H), 7.26-7.45<br>(m, 4H), 7.80-7.84 (m, 2H),<br>7.99-8.03 (m, 2H), 8.18-8.21<br>(m, 2H), 8.51-8.68 (m, 3H),<br>9.77 (s, 1H), 11.11 (s, 1H),<br>13.17 (s, 1H).                                                                                                                                                                                                                                 |
| 173 |  | A  | 763.5 | <sup>1</sup> H NMR (400 MHz, DMSO-<br>d6): δ 2.02-2.08 (m, 1H),<br>2.52-2.76 (m, 6H), 2.85-2.93<br>(m, 1H), 3.89-3.95 (m, 2H),<br>4.37-4.42 (m, 2H), 4.49 (s,<br>2H), 5.06-5.14 (m, 2H),<br>5.40-5.47 (m, 1H), 6.99 (d, J<br>= 8.4 Hz, 1H), 7.30-7.33 (m,<br>1H), 7.38-7.40 (m, 1H),<br>7.46-7.48 (m, 2H), 7.62-7.64<br>(m, 2H), 7.82-7.84 (m, 2H),<br>8.14-8.17 (m, 1H), 8.24 (d, J<br>= 2.8 Hz, 1H), 8.36-8.38 (m,<br>1H), 8.49 (d, J = 6 Hz, 1H),<br>8.58 (d, J = 2.0 Hz, 1H), 9.47<br>(s, 1H), 11.11 (s, 1H), 12.14-<br>12.28 (m, 1H).                                                                                                        |
| 174 |  | ND | 784.5 | <sup>1</sup> H NMR (400 MHz,<br>DMSO-d6): δ 1.60 (s, 6H),<br>1.62-1.69 (m, 2H), 1.77-1.82<br>(m, 2H), 2.01-2.06 (m, 1H),<br>2.30-2.44 (m, 4H), 2.54-2.67<br>(m, 2H), 2.84-2.93 (m, 1H),<br>3.31 (br, 2H), 3.38 (s, 2H),<br>3.45 (t, J = 6.4 Hz, 2H), 3.96<br>(s, 3H), 4.20 (t, J = 6.4 Hz<br>,3H), 5.11 (dd, J = 12.8 Hz<br>,1H), 5.28-5.34 (m, 1H), 6.94<br>(d, J = 8.8 Hz ,1H), 7.35 (dd,<br>J = 8.4 Hz ,1H), 7.42(s, 1H),<br>7.61-7.64 (m, 2H), 7.83 (d, J<br>= 8.4Hz ,1H), 7.99 (s, 1H),<br>8.19 (dd, J = 8.4 Hz ,1H),<br>8.32 (d, J = 8.0 Hz ,1H), 8.50<br>(d, J = 5.6 Hz ,1H), 8.64 (d, J<br>= 2.4 Hz ,1H), 9.37 (s, 1H),<br>11.11 (s, 1H). |
| 175 |  | C  | 797.5 | <sup>1</sup> H NMR (400 Hz, D6-<br>DMSO): δ1.44-1.58 (m, 5H),<br>1.75-1.79 (m, 2H), 1.92 (s,<br>6H), 2.01-2.05 (m, 2H),<br>2.50-2.61 (m, 2H), 2.83-2.94<br>(m, 1H), 3.40 (t, J = 6.4 Hz,<br>2H), 3.86-3.89 (m, 1H), 3.96                                                                                                                                                                                                                                                                                                                                                                                                                          |

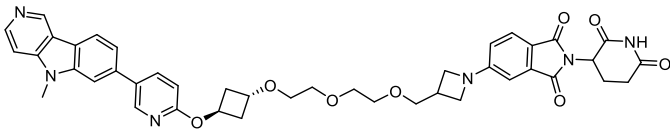
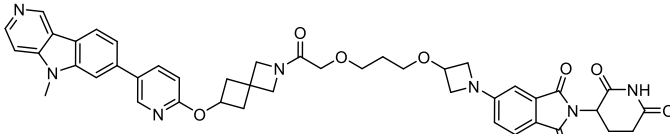
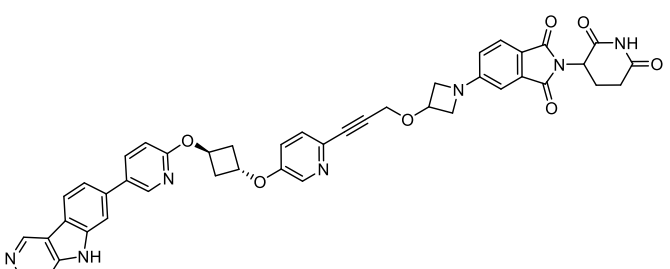
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-----|-------------------------------------------------------------------------------------|---|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | (s, 3H), 4.17 (t, J = 6.4 Hz, 2H),4.22-4.25 (m, 1H), 4.29-4.34 (m, 1H), 4.67-4.72 (m, 1H), 5.08-5.13 (m, 1H), 5.41-5.43 (m, 1H), 7.03 (d, J = 8.8 Hz, 1H), 7.34 (dd, J = 1.6, 8.4 Hz, 1H), 7.42 (s, 1H), 7.62 (d, J = 6.4 Hz, 2H), 7.82 (d, J = 8.4 Hz, 1H), 7.99 (s, 1H), 8.24 (dd, J = 2.4, 8.8 Hz, 1H), 8.33 (d, J = 8.4 Hz, 1H), 8.50 (d, J = 5.6 Hz, 1H), 8.65 (d, J = 2.0 Hz 1H), 9.36 (s, 1H), 11.10 (s, 1H).                                                                                                                                                                      |
| 176 |   | C | 809.5 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.71-1.81 (m, 4H), 1.97-2.01 (m, 1H), 2.33-2.37 (m, 2H), 2.40-2.46 (m, 2H), 2.54-2.58 (m, 2H), 2.82-2.91 (m, 1H), 3.38 (t, J = 6.4 Hz, 2H), 3.43-3.49 (m, 6H), 3.81-3.84 (m, 2H), 3.94 (s, 3H), 4.16-4.25 (m, 3H), 4.43-4.48 (m, 1H), 5.01-5.06 (m, 1H), 5.30-5.36 (m, 1H), 6.61-6.64 (m, 1H), 6.77 (d, J = 1.6 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.69-7.72 (m, 2H), 8.05 (d, J = 8.8 Hz, 1H), 8.49 (s, 1H), 8.58 (d, J = 6.0 Hz, 1H), 9.24 (s, 1H), 11.06 (s, 1H).                                      |
| 177 |  | A | 759.6 | <sup>1</sup> H NMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.71-1.80 (m, 4H), 1.90-1.93 (m, 1H), 2.28-2.37 (m, 3H), 2.40-2.44 (m, 2H), 2.56-2.57 (m, 1H), 2.83-2.92 (m, 1H), 3.37 (t, J = 6.0 Hz, 2H), 3.43-3.48 (m, 6H), 3.67-3.70 (m, 2H), 3.95 (s, 3H), 4.11-4.19 (m, 4H), 4.23-4.27 (m, 1H), 4.42-4.44 (m, 1H), 4.99-5.03 (m, 1H), 5.31-5.34 (m, 1H), 6.46-6.49 (m, 2H), 6.94 (d, J = 8.8 Hz, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.60-7.63 (m, 2H), 7.97 (s, 1H), 8.17-8.20 (m, 1H), 8.32 (d, J = 8.0 Hz, 1H), 8.50 (d, J = 6.0 Hz, 1H), 8.64 (d, J = 2.0 Hz, 1H), 9.37(s, 1H), 10.92 (s, 1H). |
| 178 |  | A | 771.6 | <sup>1</sup> HNMR (400 MHz, DMSO-d <sub>6</sub> ): δ 1.32 (s, 4H), 1.50-1.52 (m, 4H), 2.00-2.04 (m, 1H), 2.31-2.44 (m, 5H), 2.55-2.60 (m, 1H), 2.83-2.90 (m, 1H), 2.95-3.02 (m, 1H), 3.28-3.31 (m, 2H), 3.42-3.45 (m, 2H), 3.57-3.59 (m, 2H), 3.73-3.77 (m, 2H), 4.06-4.10 (m, 2H), 4.14-4.20 (m, 4H), 5.02-5.07                                                                                                                                                                                                                                                                          |

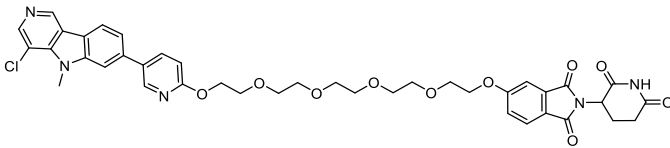
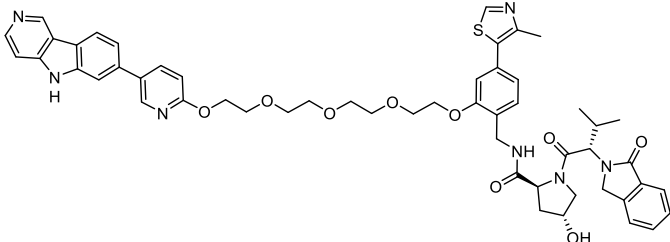
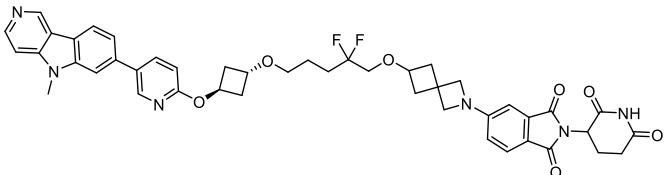
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|-----|-------------------------------------------------------------------------------------|---|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | (m, 1H), 5.32-5.34 (m, 1H), 6.61-6.63 (m, 1H), 6.76 (s, 1H), 6.96-6.99 (m, 1H), 7.59-7.61 (m, 1H), 7.85-7.87 (m, 1H), 8.20-8.26 (m, 3H), 8.52-8.55 (m, 1H), 8.70 (br, 1H), 8.76-8.78 (m, 1H), 9.77 (s, 1H), 11.06 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                  |
| 179 |    | A | 777.5 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> 6): δ 2.02-2.08 (m, 1H), 2.55-2.73 (m, 6H), 2.84-2.91 (m, 1H), 3.89-3.93 (m, 2H), 3.97 (s, 3H), 4.36-4.42 (m, 2H), 4.49 (s, 2H), 5.05-5.15 (m, 2H), 5.44 (s, 1H), 7.00 (d, <i>J</i> = 8.8 Hz, 1H), 7.30-7.33 (m, 1H), 7.37-7.40 (m, 1H), 7.45-7.49 (m, 2H), 7.63-7.67 (m, 2H), 7.83 (d, <i>J</i> = 8.4 Hz, 1H), 8.00 (s, 1H), 8.20-8.25 (m, 2H), 8.34 (d, <i>J</i> = 8.4 Hz, 1H), 8.52 (d, <i>J</i> = 6.0 Hz, 1H), 8.65 (d, <i>J</i> = 2.0 Hz, 1H), 9.39 (s, 1H), 11.11 (s, 1H).                                                                                |
| 180 |  | A | 705.4 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> 6): δ 1.97-2.00 (m, 1H), 2.33-2.44 (m, 2H), 2.55-2.67 (m, 4H), 2.86-2.96 (m, 1H), 4.29 (d, <i>J</i> = 17.2 Hz, 1H), 4.42 (d, <i>J</i> = 16.8 Hz, 1H), 5.06-5.10 (m, 2H), 5.18 (s, 2H), 5.42-5.45 (m, 1H), 6.99 (d, <i>J</i> = 8.4 Hz, 1H), 7.17 (d, <i>J</i> = 8.0 Hz, 1H), 7.29-7.33 (m, 2H), 7.50 (d, <i>J</i> = 8.4 Hz, 1H), 7.68 (d, <i>J</i> = 8.0 Hz, 2H), 7.74 (d, <i>J</i> = 5.6 Hz, 1H), 7.89 (s, 1H), 8.16 (d, <i>J</i> = 7.6 Hz, 1H), 8.24 (s, 1H), 8.41 (d, <i>J</i> = 7.6 Hz, 1H), 8.53-8.59 (m, 2H), 9.56 (s, 1H), 10.97 (s, 1H), 12.54 (br, 1H). |
| 181 |  | B | 771.6 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> 6): δ 1.34-1.41 (m, 2H), 1.48-1.57 (m, 4H), 1.84-1.89 (m, 2H), 1.95-1.99 (m, 1H), 2.31-2.46 (m, 5H), 2.54-2.58 (m, 2H), 2.79-2.92 (m, 2H), 3.35-3.42 (m, 4H), 3.68-3.71 (m, 2H), 3.95 (s, 3H), 4.11-4.19 (m, 3H), 5.01-5.05 (m, 1H), 5.29-5.35 (m, 1H), 6.59 (d, <i>J</i> = 8.0 Hz, 1H), 6.73 (s, 1H), 6.93 (d, <i>J</i> = 8.0 Hz, 1H), 7.59-7.62 (m, 3H), 7.96 (s, 1H), 8.16-8.19 (m, 1H), 8.30-8.32 (d, <i>J</i> = 8.0 Hz, 1H), 8.49 (d, <i>J</i> = 8.0 Hz, 1H), 8.61-8.62 (m, 1H), 9.35 (s, 1H), 11.06 (s, 1H).                                              |

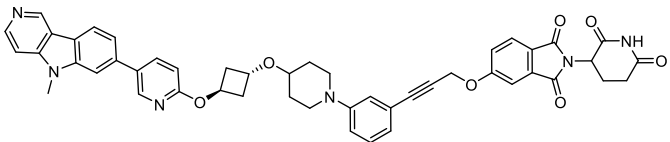
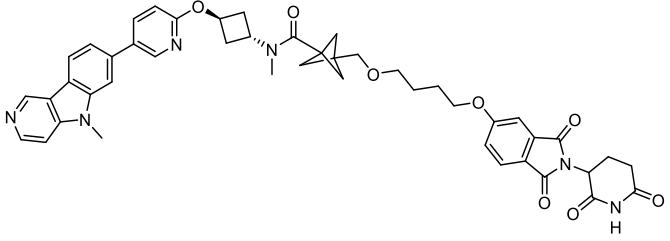
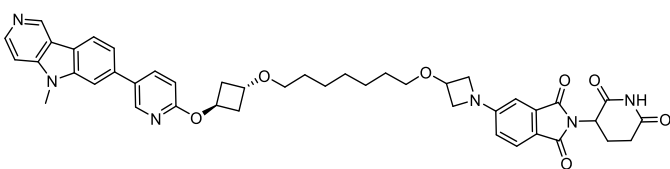
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-----|-------------------------------------------------------------------------------------|---|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 182 |    | A | 759.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.73-1.79 (m, 4H), 1.97-2.00 (m, 1H), 2.33-2.45 (m, 5H), 2.54-2.58 (m, 1H), 2.82-2.90 (m, 1H), 3.37 (t, <i>J</i> = 6.4 Hz, 2H), 3.43-3.49 (m, 6H), 3.81-3.84 (m, 2H), 4.16-4.20 (m, 1H), 4.22-4.26 (m, 2H), 4.43-4.47 (m, 1H), 5.02-5.06 (m, 1H), 5.31-5.34 (m, 1H), 6.63 (d, <i>J</i> = 8.4 Hz, 1H), 6.78 (s, 1H), 6.93 (d, <i>J</i> = 8.4 Hz, 1H), 7.60-7.65 (m, 2H), 7.72 (d, <i>J</i> = 6.0 Hz, 1H), 7.86 (s, 1H), 8.11-8.14 (m, 1H), 8.39 (d, <i>J</i> = 8.4 Hz, 1H), 8.53 (d, <i>J</i> = 6.0 Hz, 1H), 8.57 (d, <i>J</i> = 2.0 Hz, 1H), 9.53 (s, 1H), 11.06 (s, 1H), 12.42 (s, 1H).</p>        |
| 183 |  | A | 719.4 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 2.03-2.07 (m, 1H), 2.18-2.24 (m, 2H), 2.54-2.62 (m, 1H), 2.84-2.94 (m, 1H), 3.17-3.20 (m, 3H), 4.67 (t, <i>J</i> = 6.4 Hz, 1H), 5.01 (t, <i>J</i> = 6.8 Hz, 1H), 5.11-5.15 (m, 1H), 5.32 (s, 2H), 6.97 (d, <i>J</i> = 8.4 Hz, 1H), 7.33-7.36 (m, 1H), 7.45-7.52 (m, 2H), 7.58 (d, <i>J</i> = 1.6 Hz, 1H), 7.68 (d, <i>J</i> = 8.0 Hz, 1H), 7.74 (d, <i>J</i> = 5.6 Hz, 1H), 7.89 (s, 1H), 7.91 (s, 1H), 8.14-8.16 (m, 1H), 8.25 (d, <i>J</i> = 2.8 Hz, 1H), 8.41 (d, <i>J</i> = 8.4 Hz, 1H), 8.54-8.55 (m, 1H), 8.58 (d, <i>J</i> = 2.4 Hz, 1H), 9.56 (s, 1H), 11.12 (s, 1H), 12.49 (s, 1H).</p>    |
| 184 |  | A | 795.6 | <p><sup>1</sup>H NMR (400 Hz, D<sub>6</sub>-DMSO): δ 1.30-1.50 (m, 8H), 1.72-1.79 (m, 2H), 1.84 (s, 6H), 1.97-2.06 (m, 2H), 2.56-2.67 (m, 2H), 2.84-2.93 (m, 1H), 3.85-3.88 (m, 1H), 3.99 (s, 3H), 4.13-4.18 (m, 3H), 4.21-4.24 (m, 1H), 4.29-4.33 (m, 1H), 4.67-4.71 (m, 1H), 5.09-5.13 (m, 1H), 5.41-5.45 (m, 1H), 7.06 (d, <i>J</i> = 8.8 Hz, 1H), 7.34 (d, <i>J</i> = 8.0 Hz, 1H), 7.41 (s, 1H), 7.66 (d, <i>J</i> = 8.4 Hz, 1H), 7.62 (d, <i>J</i> = 5.6 Hz, 1H), 7.82 (d, <i>J</i> = 8.4 Hz, 1H), 8.04 (s, 1H), 8.23-8.29 (m, 1H), 8.37 (d, <i>J</i> = 8.0 Hz, 1H), 8.55 (d, <i>J</i> = 5.6 Hz, 1H), 8.66 (s, 1H), 9.44 (s, 1H), 11.11 (s, 1H).</p> |

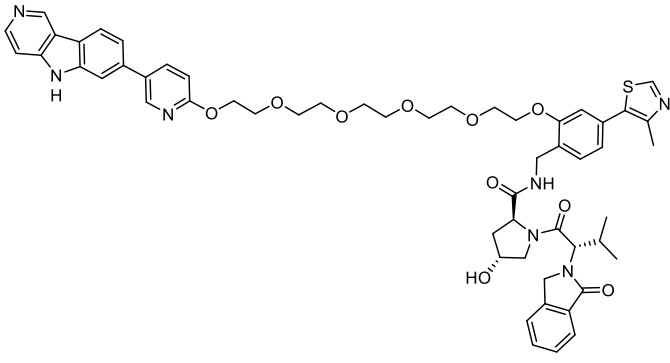
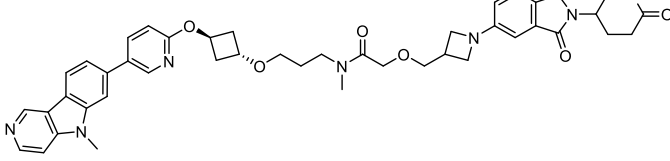
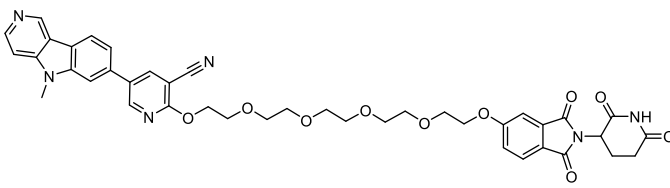
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-----|-------------------------------------------------------------------------------------|---|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 185 |    | C | 836.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 0.67 (d, J = 6.8 Hz, 3H), 0.83-0.88 (m, 3H), 1.97-2.02 (m, 2H), 2.31-2.33 (m, 1H), 2.46 (s, 3H), 3.51 (s, 1H), 3.66-3.72 (m, 2H), 4.22-4.26 (m, 2H), 4.34-4.42 (m, 4H), 4.49-4.51 (m, 2H), 4.68 (d, J = 10.0 Hz, 1H), 5.05 (d, J = 4.4 Hz, 1H), 5.32 (t, J = 4.8 Hz, 1H), 6.58 (d, J = 9.6 Hz, 1H), 6.99 (d, J = 7.2 Hz, 1H), 7.06 (s, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.47-7.53 (m, 2H), 7.58-7.63 (m, 4H), 7.69 (d, J = 6.8 Hz, 1H), 7.77 (s, 1H), 7.96-7.99 (m, 1H), 8.31-8.33 (m, 2H), 8.40 (m, 1H), 8.48 (d, J = 6.0 Hz, 1H), 8.98 (s, 1H), 9.45 (s, 1H).</p>                                       |
| 186 |  | B | 880.6 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 0.72 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.4 Hz, 3H), 1.89-1.96 (m, 1H), 2.02-2.08 (m, 1H), 2.28-2.34 (m, 1H), 2.47 (s, 3H), 3.68-3.70 (m, 1H), 3.75-3.80 (m, 1H), 3.88-3.92 (m, 4H), 4.20-4.39 (m, 5H), 4.40-4.58 (m, 5H), 4.71 (d, J = 10.8 Hz, 1H), 5.10 (d, J = 3.6 Hz, 1H), 6.95 (d, J = 8.8 Hz, 1H), 7.02 (d, J = 7.6 Hz, 1H), 7.07 (s, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.46-7.53 (m, 1H), 7.56-7.67 (m, 4H), 7.70 (d, J = 7.6 Hz, 1H), 7.84 (s, 1H), 8.11-8.14 (m, 1H), 8.36-8.40 (m, 2H), 8.50 (d, J = 6.0 Hz, 1H), 8.58 (d, J = 2.4 Hz, 1H), 8.98 (s, 1H), 9.48 (s, 1H), 12.16-12.29 (m, 1H).</p> |
| 187 |  | C | 924.6 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 0.71 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H), 1.89-2.07 (m, 3H), 2.26-2.39 (m, 2H), 2.46 (s, 3H), 3.64-3.70 (m, 5H), 3.75-3.83 (m, 5H), 4.18-4.23 (m, 2H), 4.27-4.36 (m, 3H), 4.39-4.46 (m, 4H), 4.52-4.57 (m, 1H), 4.69-4.72 (m, 1H), 5.08 (d, J = 4.0 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 7.01 (d, J = 8.0 Hz, 1H), 7.05 (s, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.47-7.51 (m, 1H), 7.55-7.60 (m, 4H), 7.70 (d, J = 8.0 Hz, 1H), 7.80 (s, 1H), 8.09-8.11 (m, 1H), 8.31-8.34 (m, 1H), 8.36-8.39 (m, 1H), 8.45 (d, J = 4.8 Hz, 1H), 8.55 (m, 1H),</p>                                                   |

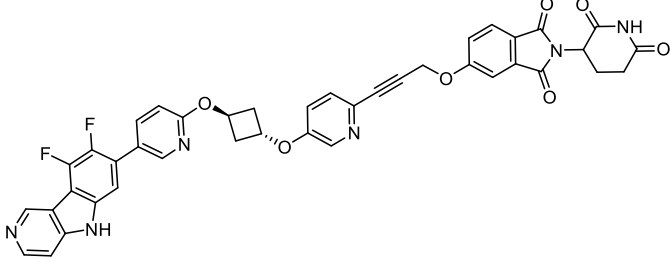
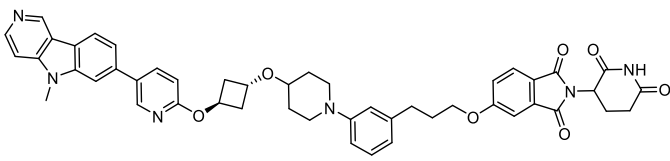
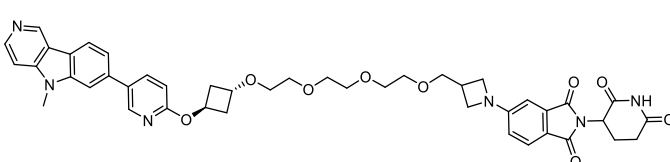
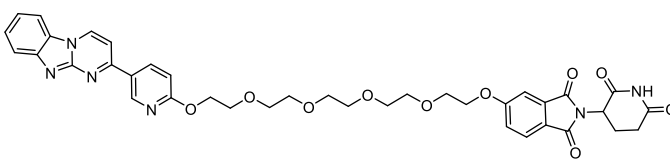
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|-----|-------------------------------------------------------------------------------------|---|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | 8.98 (s, 1H), 9.41 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| 188 |    | B | 762.5 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 2.02-2.08 (m, 1H), 2.51-2.78 (m, 6H), 2.85-2.94 (m, 1H), 3.86-3.92 (m, 2H), 4.38-4.40 (m, 2H), 4.45 (s, 2H), 4.98-5.03 (m, 1H), 5.09-5.15 (m, 1H), 5.40-5.45 (m, 1H), 6.88 (d, <i>J</i> = 8.8 Hz, 2H), 6.99 (d, <i>J</i> = 8.4 Hz, 1H), 7.36-7.40 (m, 3H), 7.47 (d, <i>J</i> = 2.0 Hz, 1H), 7.61-7.67 (m, 2H), 7.82-7.85 (m, 2H), 8.14-8.17 (m, 1H), 8.37 (d, <i>J</i> = 8.0 Hz, 1H), 8.50 (d, <i>J</i> = 6.0 Hz, 1H), 8.58 (d, <i>J</i> = 2.4 Hz, 1H), 9.48 (s, 1H), 11.12 (s, 1H), 12.22 (br, 1H). |
| 189 |  | B | 718.4 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 2.03-2.08 (m, 1H), 2.54-2.70 (m, 6H), 2.84 -2.92 (m, 1H), 4.98-5.03 (m, 1H), 5.10-5.16 (m, 1H), 5.27 (s, 2H), 5.39-5.45 (m, 1H), 6.89 (d, <i>J</i> = 8.8 Hz, 2H), 6.99 (d, <i>J</i> = 8.8 Hz, 1H), 7.40 (d, <i>J</i> = 8.8 Hz, 2H), 7.45-7.47 (m, 1H), 7.57 (d, <i>J</i> = 2.0 Hz, 1H), 7.65-7.70 (m, 2H), 7.86-7.91 (m, 2H), 8.14-8.17 (m, 1H), 8.39 (d, <i>J</i> = 8.0 Hz, 1H), 8.52 (d, <i>J</i> = 6.4 Hz, 1H), 8.58 (d, <i>J</i> = 2.4 Hz, 1H), 9.52 (s, 1H), 11.12 (s, 1H), 12.37 (s, 1H).      |
| 190 |  | C | 773.5 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 1.84-1.89 (m, 2H), 1.95-2.03 (m, 3H), 2.31-2.39 (m, 4H), 2.81-2.88 (m, 2H), 3.45-3.55 (m, 12H), 3.68 (m, 2H), 4.10 (s, 3H), 4.24 (m, 1H), 5.00-5.04 (m, 1H), 5.03 (s, 1H), 6.55-6.58 (m, 1H), 6.70 (s, 1H), 6.94-6.97 (m, 1H), 7.56-7.57 (m, 1H), 7.80-7.82 (m, 1H), 8.11-8.23 (m, 3H), 8.48-8.51 (m, 1H), 8.67-8.73 (m, 2H), 9.69 (s, 1H), 11.06 (s, 1H).                                                                                                                                           |
| 191 |  | A | 773.5 | <sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ): δ 1.72-1.78 (m, 2H), 1.95-2.01 (m, 1H), 2.31-2.46 (m, 4H), 2.54-2.67 (m, 2H), 2.82-2.91 (m, 1H), 2.95-3.02 (m, 1H), 3.44-3.52 (m, 8H), 3.58-3.60 (m, 2H), 3.73-3.76 (m, 2H), 3.97 (s, 3H), 4.07 (t, <i>J</i> = 8.0 Hz, 2H), 4.20-4.25 (m, 1H), 5.02-5.06 (m, 1H), 5.29-5.35 (m, 1H), 6.59-6.61 (m, 1H), 6.74-6.75 (m, 1H), 6.93-6.95 (d, <i>J</i> = 8.0 Hz, 1H), 7.58-7.68 (m, 3H), 7.99 (s,                                                                                                           |

|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|-----|-------------------------------------------------------------------------------------|---|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | 1H), 8.17-8.20 (m, 1H), 8.33 (d, J = 8.0 Hz, 1H), 8.52 (d, J = 8.0 Hz, 1H), 8.63-8.64 (m, 1H), 9.39 (s, 1H), 11.07 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| 192 |    | C | 759.5 | <p><sup>1</sup>HNMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.95-1.99 (m, 1H), 2.08 (s, 1H), 2.31-2.37 (m, 2H), 2.41-2.46 (m, 3H), 2.54-2.58 (m, 1H), 2.83-2.89 (m, 1H), 2.96-3.01 (m, 1H), 3.44-3.46 (m, 1H), 3.53-3.57 (m, 6H), 3.64-3.66 (m, 2H), 3.74-3.78 (m, 2H), 3.95 (s, 3H), 4.08 (t, J = 8.4 Hz, 2H), 4.21-4.23 (m, 1H), 5.01-5.06 (m, 1H), 5.30-5.33 (m, 1H), 6.60 (d, J = 9.6 Hz, 1H), 6.75 (s, 1H), 6.93 (d, J = 8.4 Hz, 1H), 7.58-7.64 (m, 3H), 7.97 (s, 2H), 8.17-8.20 (m, 1H), 8.31 (d, J = 8.0 Hz, 1H), 8.49 (d, J = 5.6 Hz, 1H), 8.62-8.63 (m, 1H), 9.36 (s, 1H), 11.06 (s, 1H);</p>                                                                        |
| 193 |  | B | 798.5 | <p><sup>1</sup>H NMR: (400 MHz, DMSO-d<sub>6</sub>)</p> <p>δ: 11.07 (br s, 1H), 9.36 (s, 1H), 8.66 - 8.58 (m, 1H), 8.49 (d, J=5.8 Hz, 1H), 8.32 (d, J=8.2 Hz, 1H), 8.23 (s, 2H), 8.18 (dd, J=2.5, 8.7 Hz, 1H), 7.97 (s, 1H), 7.66 - 7.58 (m, 3H), 6.92 (d, J=8.7 Hz, 1H), 6.81 (br d, J=2.3 Hz, 1H), 6.69 - 6.63 (m, 1H), 5.16 - 5.08 (m, 1H), 5.08 - 5.02 (m, 1H), 4.47 (br s, 1H), 4.30 - 4.22 (m, 3H), 4.19 (s, 1H), 3.99 (s, 1H), 3.95 (s, 3H), 3.95 - 3.89 (m, 4H), 3.86 (br s, 3H), 3.49 - 3.48 (m, 2H), 2.92 - 2.81 (m, 1H), 2.74 (br d, J=6.5 Hz, 2H), 2.58 (br s, 1H), 2.54 (s, 2H), 2.30 - 2.26 (m, 1H), 1.98 (br d, J=4.9 Hz, 1H), 1.85 - 1.74 (m, 2H).</p> |
| 194 |  | C | 774.5 | <p><sup>1</sup>HNMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.93-2.11 (m, 2H), 2.54-2.74 (m, 5H), 2.54-2.93 (m, 1H), 3.95-3.98 (m, 2H), 4.31-4.34 (m, 2H), 4.49 (s, 3H), 4.67-4.73 (m, 1H), 5.04-5.14 (m, 2H), 5.41-5.47 (m, 1H), 6.67-6.69 (m, 1H), 6.82-6.83 (m, 1H), 6.99 (d, J = 8.0 Hz, 1H), 7.33-7.36 (m, 1H), 7.53-7.55 (m, 1H), 7.65-7.72 (m, 3H), 7.88 (s, 3H), 8.15-8.18 (m, 1H), 8.25-8.26 (m, 1H), 8.40 (d, J</p>                                                                                                                                                                                                                                                 |

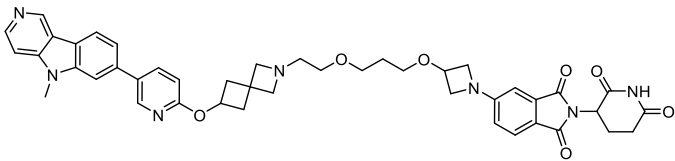
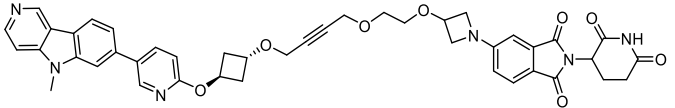
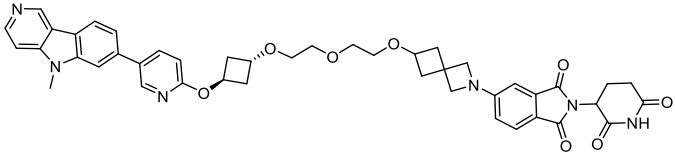
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|-----|-------------------------------------------------------------------------------------|---|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                                                     |   |       | = 8.0 Hz, 1H), 8.52-8.54 (m, 1H), 8.58-8.59 (m, 1H), 9.54 (s, 1H), 11.07 (s, 1H).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| 195 |    | A | 786.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 2.01-2.04 (m, 1H), 2.50-2.60 (m, 2H), 2.83-2.92 (m, 1H), 3.52-3.59 (m, 12H), 3.77-3.79 (m, 4H), 4.27-4.28 (m, 5H), 4.43-4.46 (m, 2H), 5.08-5.13 (m, 1H), 6.96 (d, J = 8.4 Hz, 1H), 7.32-7.34 (m, 1H), 7.41 (s, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 8.03 (s, 1H), 8.19-8.22 (m, 1H), 8.35 (d, J = 8.0 Hz, 1H), 8.44 (s, 1H), 8.64-8.65 (m, 1H), 9.22 (s, 1H), 11.10 (s, 1H).</p>                                                                                                                                                                       |
| 196 |  | C | 968.6 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 0.71 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H), 1.89-2.07 (m, 3H), 2.27-2.35 (m, 2H), 2.46 (s, 3H), 3.57-3.58 (m, 5H), 3.63-3.68 (m, 4H), 3.76-3.81 (m, 5H), 4.17-4.19 (m, 2H), 4.27-4.34 (m, 3H), 4.39-4.46 (m, 4H), 4.52-4.57 (m, 1H), 4.69-4.72 (m, 1H), 5.09 (m, 1H), 6.95 (d, J = 8.8 Hz, 1H), 7.01 (d, J = 8.8 Hz, 1H), 7.04 (s, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.47-7.51 (m, 1H), 7.60-7.64 (m, 4H), 7.70 (d, J = 8.0 Hz, 1H), 7.83 (s, 1H), 8.09-8.14 (m, 1H), 8.34-8.38 (m, 2H), 8.49 (d, J = 4.8 Hz, 1H), 8.55-8.56 (m, 1H), 8.97 (s, 1H), 9.47 (s, 1H).</p> |
| 197 |  | C | 819.5 | <p><sup>1</sup>H NMR: (400 MHz, CDCl<sub>3</sub>)</p> <p>δ: 9.37 (s, 1H), 8.61 (d, J = 6.0 Hz, 1H), 8.51 (d, J = 2.4 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 7.95 - 7.93 (m, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.59 (s, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.4 (d, J = 6.0 Hz, 1H), 6.87 (d, J = 8.0 Hz, 1H), 6.76 (d, J = 2.4 Hz, 1H), 6.50 - 6.48 (m, 1H), 5.44 - 5.41 (m, 1H), 4.96 (dd, J = 5.2, 12.4 Hz, 1H), 4.31 - 4.27 (m, 1H), 4.07 - 4.02 (m, 5H), 3.94 (s, 3H), 3.59 (t, J = 12.4 Hz, 2H), 3.47 (t, J = 6.4 Hz, 2H), 2.92 - 2.78 (m, 3H), 2.65 - 2.48 (m, 6H), 2.32 - 2.27 (m, 2H), 2.19 - 1.99 (m, 4H), 1.86 - 1.79 (m, 1H).</p> |

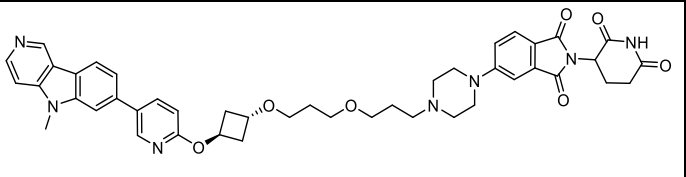
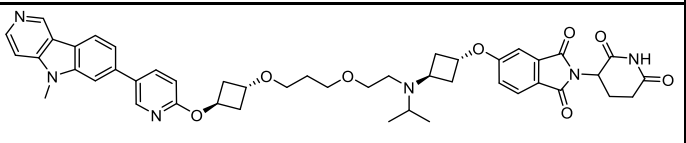
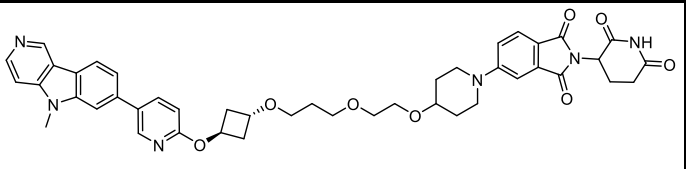
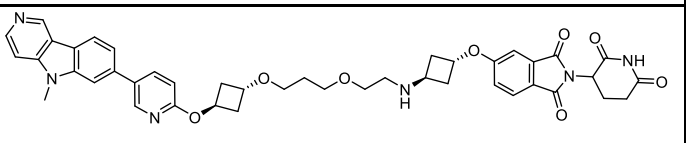
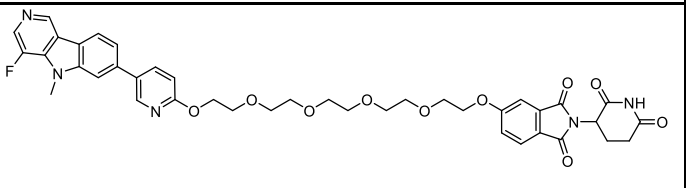
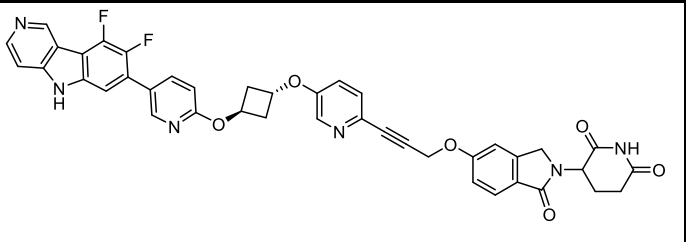
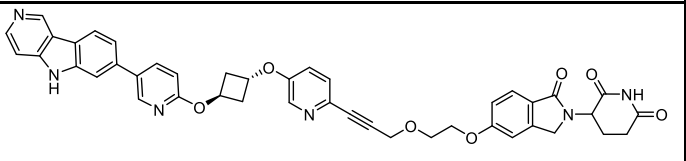
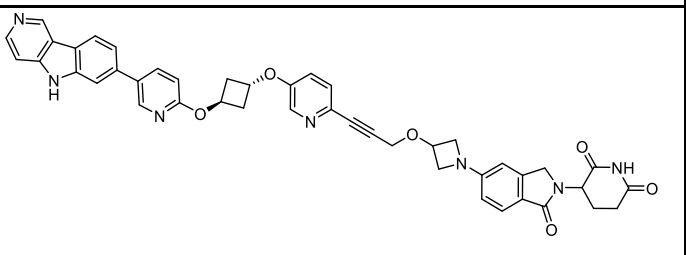
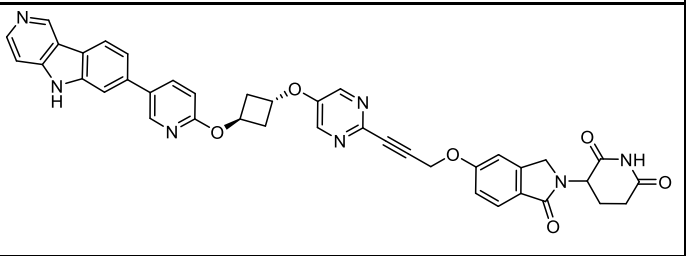
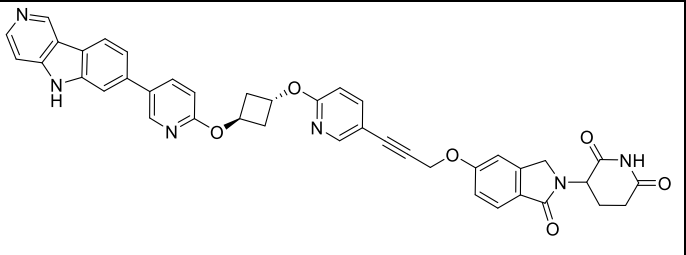
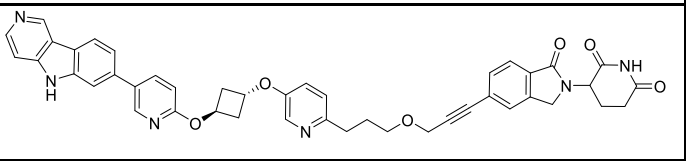
|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-----|-------------------------------------------------------------------------------------|---|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 198 |    | A | 815.5 | <p><sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ 1.46-1.55 (m, 2H), 1.84-1.94 (m, 2H), 2.03-2.07 (m, 1H), 2.35-2.46 (m, 4H), 2.58-2.62 (m, 1H), 2.85-2.94 (m, 3H), 3.50-3.56 (m, 3H), 3.99 (m, 3H), 4.38-4.44 (m, 1H), 5.11-5.16 (m, 1H), 5.28 (s, 2H), 5.31-5.34 (m, 1H), 6.80-6.82 (m, 1H), 6.95-7.01 (m, 3H), 7.18-7.22 (m, 1H), 7.45-7.48 (m, 1H), 7.57-7.58 (m, 1H), 7.66-7.68 (m, 1H), 7.75-7.81 (m, 1H), 7.89-7.91 (m, 1H), 8.03 (s, 1H), 8.19-8.22 (m, 1H), 8.36-8.66 (m, 3H), 9.42 (br, 1H), 11.12 (s, 1H).</p>                                                                             |
| 199 |  | C | 811.6 | <p><sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 1.71-1.98 (m, 6H), 2.06-2.15 (m, 8H), 2.46-2.57 (m, 2H), 2.57-2.88 (m, 4H), 2.96-3.10 (m, 2H), 3.43-3.56 (m, 3H), 3.94 (s, 3H), 4.05-4.20 (m, 2H), 4.91-5.01 (m, 1H), 5.05-5.26 (m, 1H), 5.31-5.42 (m, 1H), 6.82-6.94 (m, 1H), 7.14-7.23 (m, 1H), 7.31-7.45 (m, 2H), 7.48-7.65 (m, 2H), 7.73-7.81 (m, 1H), 7.89-7.99 (m, 1H), 8.19-8.28 (m, 1H), 8.38-8.67 (m, 3H), 9.32-9.42 (m, 1H).</p>                                                                                                                                                          |
| 200 |  | A | 711.6 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.23 (s, 4H), 1.50-1.54 (m, 4H), 1.97-2.03 (m, 2H), 2.33-2.37 (m, 2H), 2.40-2.46 (m, 2H), 2.54-2.67 (m, 2H), 2.83-2.92 (m, 2H), 3.31 (t, J = 6.4 Hz, 2H), 3.41 (t, J = 6.4 Hz, 2H), 3.82-3.85 (m, 2H), 4.14 (s, 3H), 4.16-4.26 (m, 3H), 4.43-4.48 (m, 1H), 5.03-5.07 (m, 1H), 5.32-5.35 (m, 1H), 6.63-6.66 (m, 1H), 6.78 (s, 1H), 6.98 (d, J = 8.8 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 8.20-8.26 (m, 3H), 8.53 (d, J = 8.4 Hz, 1H), 8.70 (d, J = 2.0 Hz, 1H), 8.76 (d, J = 6.8 Hz, 1H), 9.76 (s, 1H), 11.07 (s, 1H).</p> |

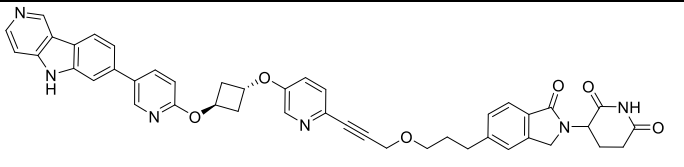
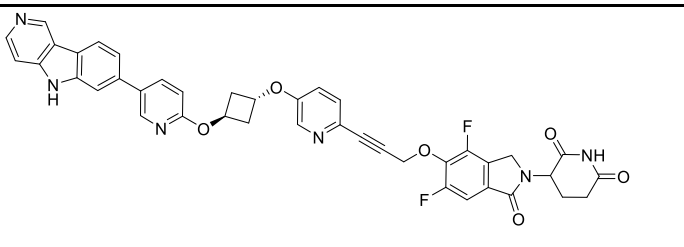
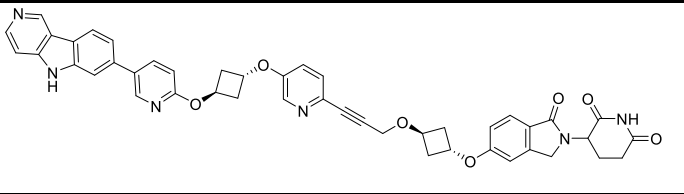
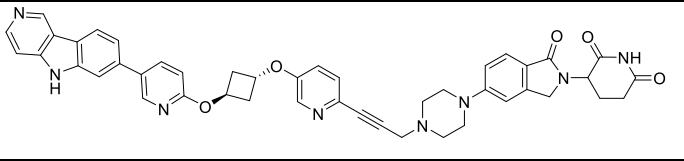
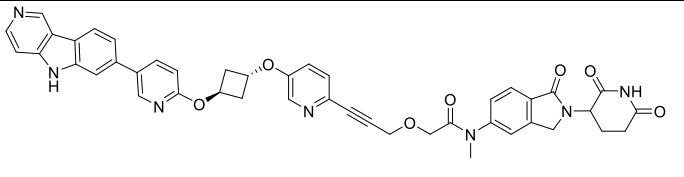
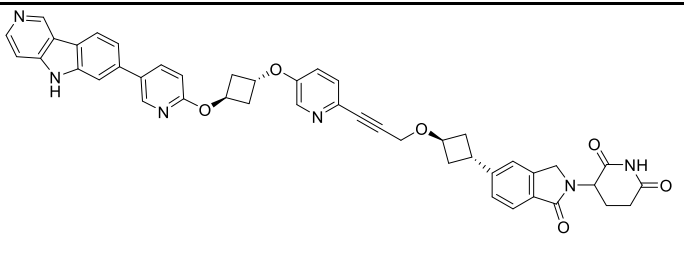
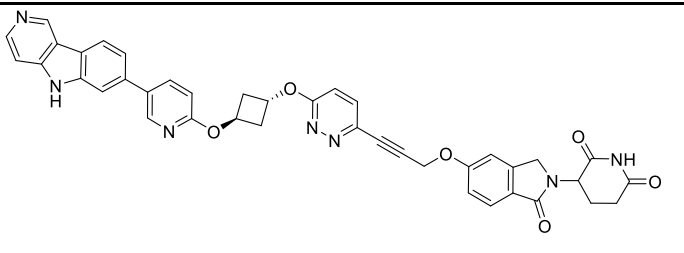
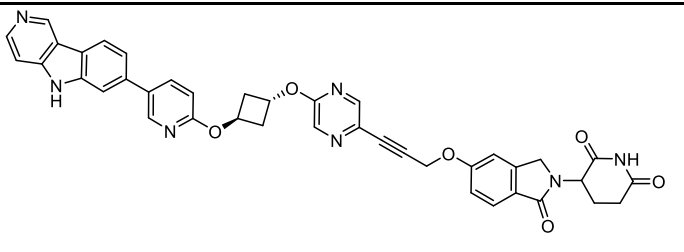
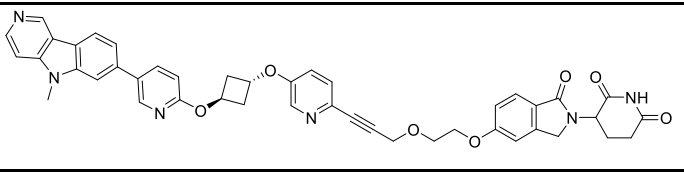
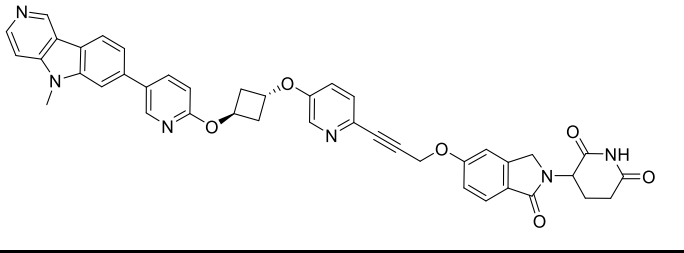
|     |                                                                                     |   |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-----|-------------------------------------------------------------------------------------|---|--------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 201 |    | C | 1012.7 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 0.72 (d, J = 6.4 Hz, 3H), 0.95 (d, J = 6.4 Hz, 3H), 1.89-1.95 (m, 1H), 2.03-2.08 (m, 1H), 2.16-2.35 (m, 2H), 2.46 (s, 3H), 3.52-3.58 (m, 10H), 3.62-3.70 (m, 4H), 3.77-3.78 (m, 5H), 4.14-4.21 (m, 2H), 4.27-4.34 (m, 3H), 4.39-4.47 (m, 4H), 4.52-4.57 (m, 1H), 4.70-4.72 (m, 1H), 5.09-5.10 (m, 1H), 6.95-7.04 (m, 3H), 7.34 (d, J = 8.0 Hz, 1H), 7.47-7.51 (m, 1H), 7.58-7.62 (m, 2H), 7.65-7.73 (m, 3H), 7.87 (s, 1H), 8.11-8.14 (m, 1H), 8.36-8.40 (m, 2H), 8.53 (d, J = 6.4 Hz, 1H), 8.56-8.58 (m, 1H), 8.97 (s, 1H), 9.54 (s, 1H).</p> |
| 202 |  | B | 800.6  | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.66-1.82 (m, 3H), 1.95-2.00 (m, 1H), 2.28-2.47 (m, 6H), 2.54-2.60 (m, 1H), 2.81-2.91 (m, 4H), 2.97-3.11 (m, 2H), 3.34-3.38 (m, 1H), 3.66-3.69 (m, 2H), 3.78-3.86 (m, 2H), 3.96 (s, 3H), 4.07-4.11 (m, 2H), 4.19-4.23 (m, 3H), 5.00-5.07 (m, 1H), 5.29-5.35 (m, 1H), 6.58-6.64 (m, 1H), 6.73-6.78 (m, 1H), 6.91-6.96 (m, 1H), 7.57-7.67 (m, 3H), 7.95-8.00 (m, 1H), 8.15-8.21 (m, 1H), 8.29-8.35 (m, 1H), 8.48-8.54 (m, 1H), 8.60-8.66 (m, 1H), 9.38 (s, 1H), 11.05 (s, 1H).</p>                                                              |
| 203 |  | A | 777.5  | <p><sup>1</sup>H NMR: (400 MHz, DMSO-d<sub>6</sub>): δ: 11.13 (s, 1H), 9.37 (s, 1H), 8.96 (d, J = 2.5 Hz, 1H), 8.81 (d, J = 2.5 Hz, 1H), 8.51 (d, J = 5.8 Hz, 1H), 8.35 (d, J = 8.2 Hz, 1H), 8.25 (s, 1H), 8.10 (d, J = 0.9 Hz, 1H), 7.79 (d, J = 8.3 Hz, 1H), 7.74 - 7.67 (m, 1H), 7.63 (d, J = 5.6 Hz, 1H), 7.41 (d, J = 2.1 Hz, 1H), 7.33 (dd, J = 2.3, 8.3 Hz, 1H), 5.19 - 5.04 (m, 1H), 4.60 (dd, J = 3.9, 5.4 Hz, 2H), 4.32 - 4.22 (m, 2H), 3.96 (s, 3H), 3.86 - 3.81 (m, 2H), 3.79 - 3.74 (m, 2H), 3.65 - 3.52 (m, 12H), 2.92 - 2.82 (m, 1H), 2.63 - 2.54 (m, 2H), 2.07 - 1.97 (m, 1H)</p>   |

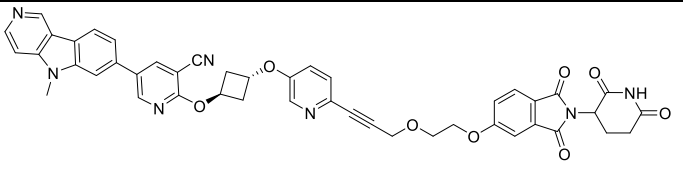
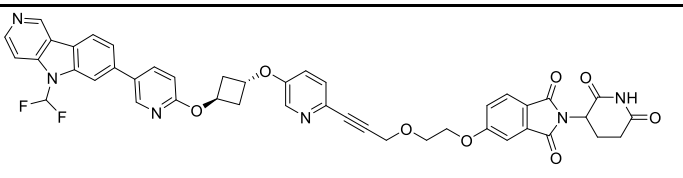
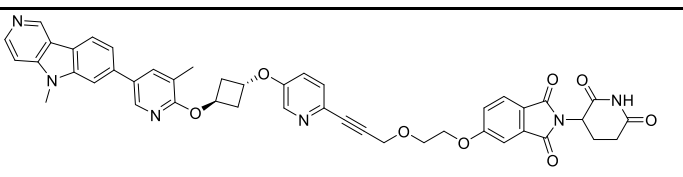
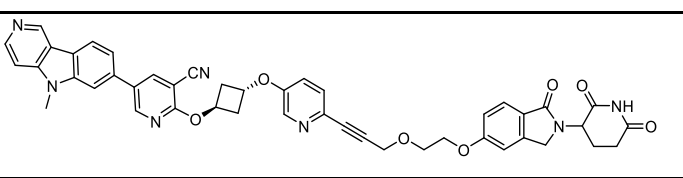
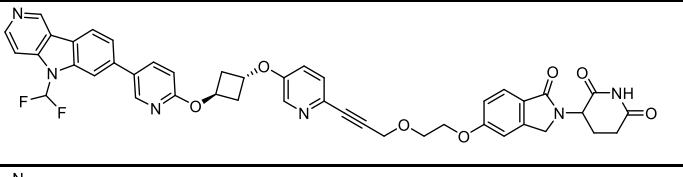
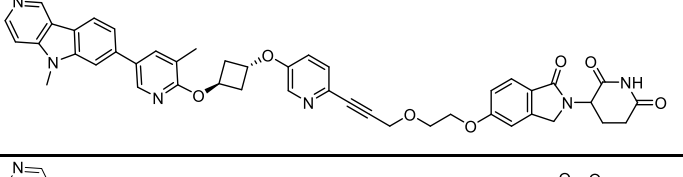
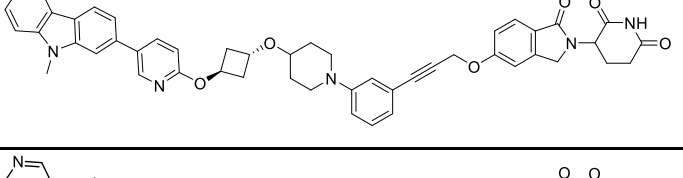
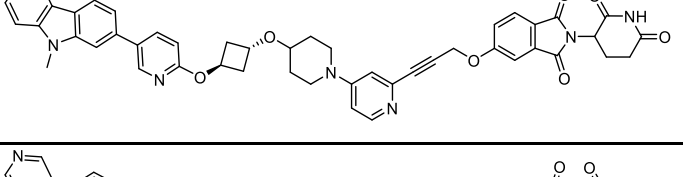
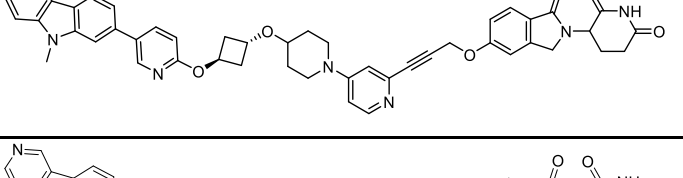
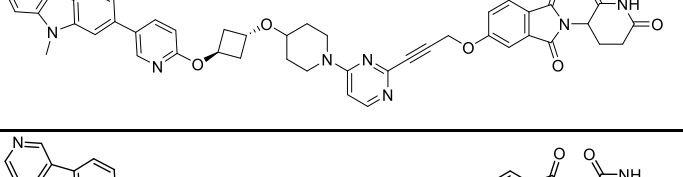
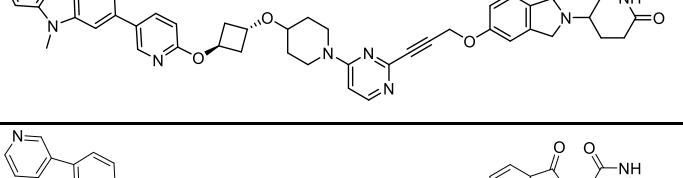
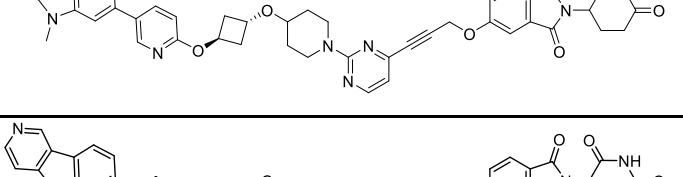
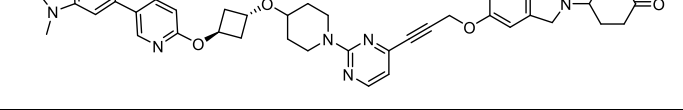
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| 204 |    | C | 755.4 | <p><sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 1.98-2.03 (m, 2H), 2.18-2.22 (m, 2H), 2.69-2.77 (m, 4H), 5.33-5.36 (m, 1H), 5.48-5.52 (m, 1H), 6.86 (d, J = 8.4 Hz, 1H), 7.05 (dd, J = 2.4, 8.4Hz, 1H), 7.22 (d, J = 4.8 Hz, 1H), 7.32 (dd, J = 2.0, 8.4Hz, 1H), 7.37 (d, J = 7.2Hz, 2H), 7.49 (d, J = 1.6 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.8 Hz, 1H), 8.20 (d, J = 2.8 Hz, 1H), 8.35 (s, 1H), 8.57 (d, J = 6.0 Hz, 1H), 9.38 (s, 1H).</p>                                                                                                                                                             |
| 205 |  | A | 819.6 | <p><sup>1</sup>HNMR (400 MHz, CD<sub>3</sub>OD): δ 1.44-1.58 (m, 2H), 1.84-1.91 (m, 2H), 2.04-2.07 (m, 3H), 2.34-2.44 (m, 4H), 2.62-2.93 (m, 7H), 3.46-3.49 (m, 2H), 3.99 (m, 3H), 4.14-4.17 (m, 2H), 4.39-4.42 (m, 1H), 5.11-5.15 (m, 1H), 5.32-5.34 (m, 1H), 6.63-6.64 (m, 1H), 6.75-6.78 (m, 2H), 6.95-6.97 (m, 1H), 7.09-7.13 (m, 1H), 7.36-7.38 (m, 1H), 7.43 (s, 1H), 7.66-7.73 (m, 2H), 7.83-7.85 (m, 1H), 8.02 (s, 1H), 8.20-8.22 (m, 1H), 8.36-8.38 (m, 1H), 8.53-8.55 (m, 1H), 8.66 (s, 1H), 9.43 (s, 1H), 11.12 (s, 1H).</p>                                                                                     |
| 206 |  | B | 803.6 | <p><sup>1</sup>HNMR (400 MHz, DMSO-d<sub>6</sub>): δ 1.97-2.00 (m, 1H), 2.32-2.37 (m, 2H), 2.42-2.46 (m,2H), 2.54-2.58 (m, 2H), 2.82-2.91 (m, 1H), 2.95-3.01 (m, 1H), 3.44-3.46 (m, 2H), 3.53-3.56 (m, 10H), 3.62-3.64 (m, 2H), 3.72-3.75 (m, 2H), 4.02 (s, 3H), 4.06 (t, J = 8.0 Hz, 2H), 4.20-4.24 (m, 1H), 5.02-5.06 (m, 1H), 5.29-5.34 (m, 1H), 6.58-6.60 (m, 1H), 6.73-6.75 (m, 1H), 6.95 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.82-7.84 (m, 1H), 8.06 (s, 1H), 8.19-8.22 (m, 1H), 8.39 (d, J = 8.0 Hz, 1H), 8.58-8.59 (m, 1H), 8.65-8.66 (m, 1H), 9.49 (s, 1H), 11.07(s, 1H).</p> |
| 207 |  | B | 739.5 | <p><sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ: 11.13 (s, 1H), 9.57 (d, J = 7.2 Hz, 1H), 9.13 (d, J = 2.4 Hz, 1H), 8.63 (dd, J = 2.5, 8.8 Hz, 1H), 8.31 (d, J = 8.2 Hz, 1H), 7.87 - 7.77 (m, 3H), 7.59 - 7.48 (m, 1H),</p>                                                                                                                                                                                                                                                                                                                                                                                           |



|     |                                                                                     |   |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-----|-------------------------------------------------------------------------------------|---|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 211 |    | C | 784.6 | <p><sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ: 9.33 (s, 1H), 8.59 (d, J = 5.6 Hz, 1H), 8.47 (d, J = 2.1 Hz, 1H), 8.21 (d, J = 8.2 Hz, 1H), 7.92 (dd, J = 2.3, 8.3 Hz, 1H), 7.65 (d, J = 8.2 Hz, 1H), 7.55 (s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 6.0 Hz, 1H), 6.86 - 6.77 (m, 2H), 6.55 (br d, J = 6.8 Hz, 1H), 5.17 (quin, J = 6.9 Hz, 1H), 4.93 (dd, J = 5.1, 12.0 Hz, 1H), 4.49 (br s, 1H), 4.25 (br t, J = 7.5 Hz, 2H), 3.96 - 3.84 (m, 5H), 3.57 - 3.35 (m, 10H), 2.93 - 2.66 (m, 7H), 2.39 - 2.27 (m, 2H), 2.16 - 2.08 (m, 1H), 1.93 - 1.82 (m, 2H).</p>                                                                                |
| 212 |  | A | 769.5 | <p><sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ: 9.39 (s, 1H), 8.61 (d, J=6.0 Hz, 1H), 8.52 - 8.43 (m, 2H), 8.32 - 8.04 (m, 2H), 7.93 (dd, J=2.6, 8.6 Hz, 1H), 7.63 (d, J=8.3 Hz, 1H), 7.59 (s, 1H), 7.53 (dd, J=1.4, 8.1 Hz, 1H), 7.42 (d, J=6.0 Hz, 1H), 6.85 (d, J=8.5 Hz, 1H), 6.78 (d, J=2.0 Hz, 1H), 6.52 (dd, J=2.1, 8.3 Hz, 1H), 5.46 - 5.35 (m, 1H), 4.93 (dd, J=5.2, 12.4 Hz, 1H), 4.61 - 4.43 (m, 2H), 4.29 - 4.27 (m, 2H), 4.27 - 4.21 (m, 2H), 4.20 - 4.16 (m, 2H), 4.00 - 3.89 (m, 5H), 3.78 - 3.63 (m, 4H), 2.92 - 2.67 (m, 3H), 2.64 - 2.55 (m, 2H), 2.51 (td, J=3.5, 7.0 Hz, 2H), 2.16 - 2.08 (m, 1H).</p>                              |
| 213 |  | C | 785.5 | <p><sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ: 9.38 (s, 1H), 8.59 (d, J = 5.9 Hz, 1H), 8.48 (d, J = 2.3 Hz, 2H), 8.22 (d, J = 8.0 Hz, 1H), 7.92 (dd, J = 2.6, 8.5 Hz, 1H), 7.61 - 7.55 (m, 2H), 7.49 (dd, J = 1.3, 8.1 Hz, 1H), 7.40 (d, J = 6.0 Hz, 1H), 6.85 (d, J = 8.5 Hz, 1H), 6.72 (d, J = 2.0 Hz, 1H), 6.45 (dd, J = 2.1, 8.3 Hz, 1H), 5.47 - 5.35 (m, 1H), 4.92 (dd, J = 5.3, 12.2 Hz, 1H), 4.39 - 4.27 (m, 1H), 4.07 - 3.95 (m, 5H), 3.93 (s, 3H), 3.72 - 3.64 (m, 4H), 3.57 (ddd, J = 3.7, 5.8, 11.9 Hz, 4H), 2.91 - 2.76 (m, 3H), 2.59 (ddd, J = 4.0, 6.9, 13.4 Hz, 4H), 2.52 - 2.43 (m, 2H), 2.32 - 2.23 (m, 2H), 2.16 - 2.07 (m, 1H).</p> |

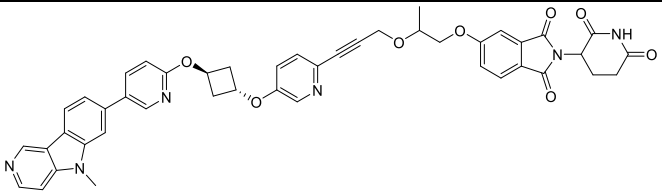
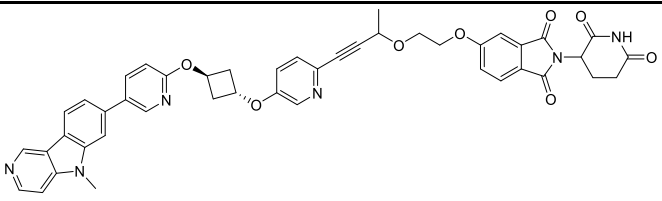
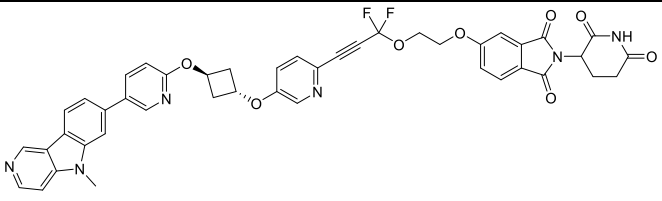
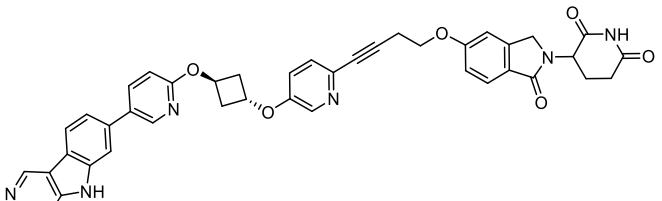
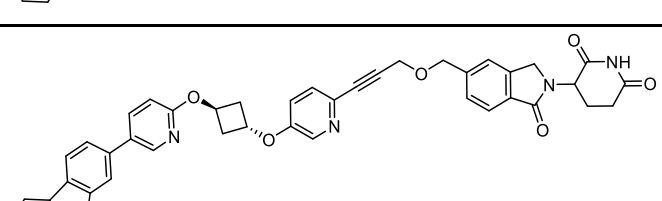
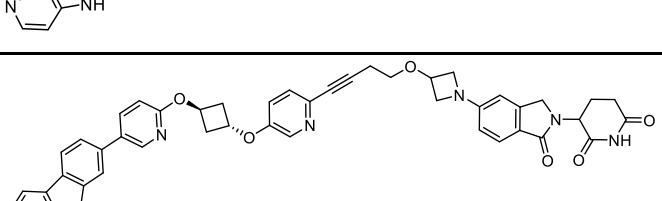
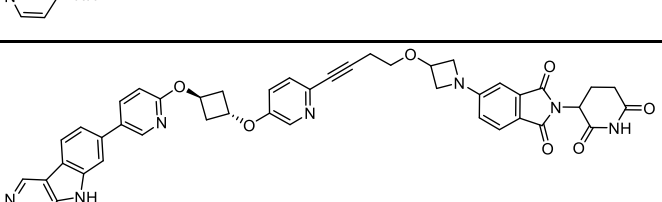
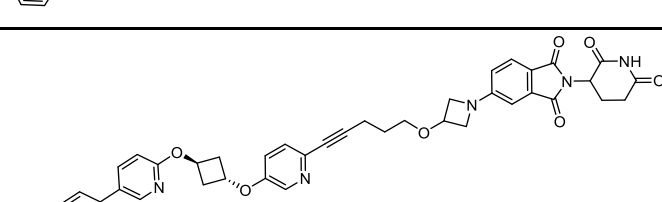
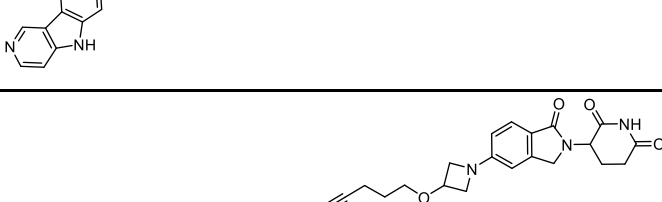
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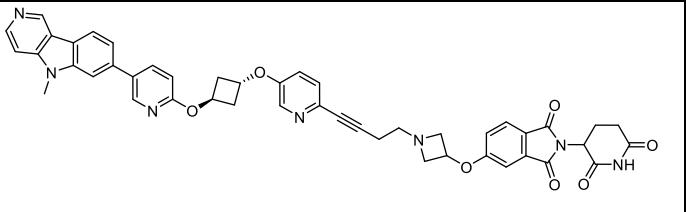
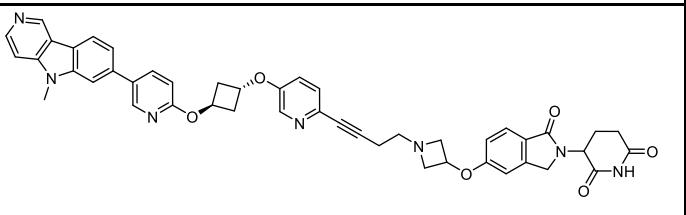
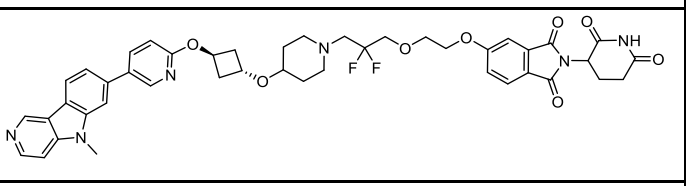
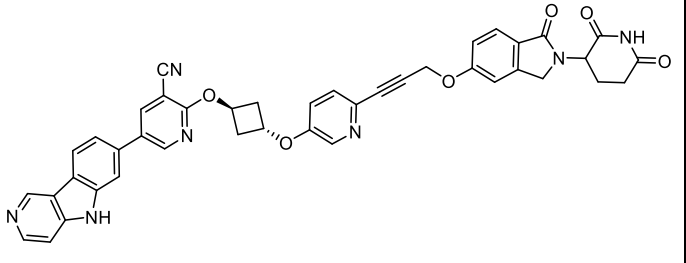
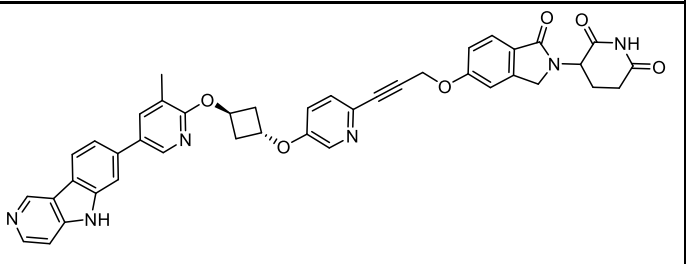
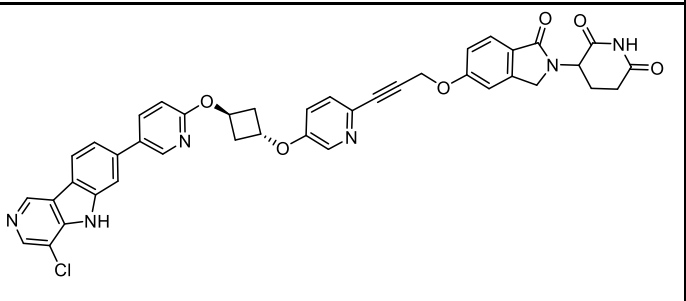
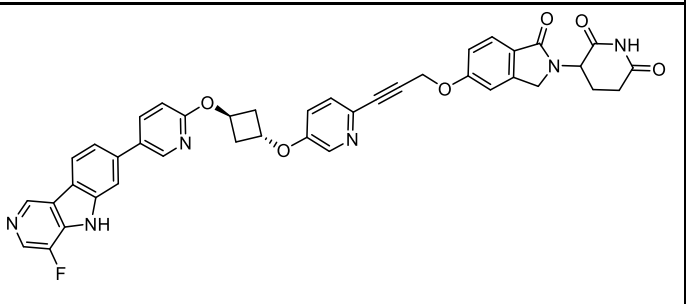
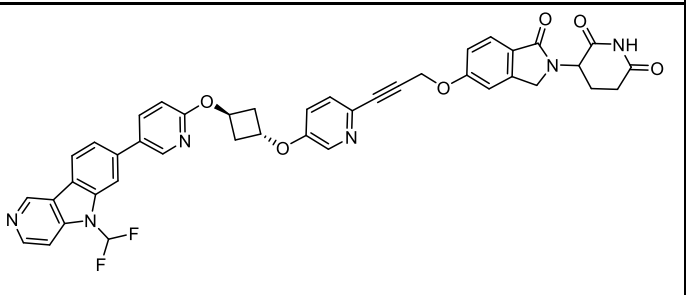
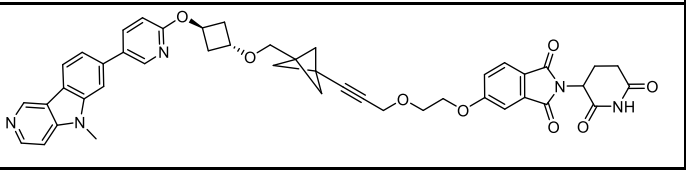
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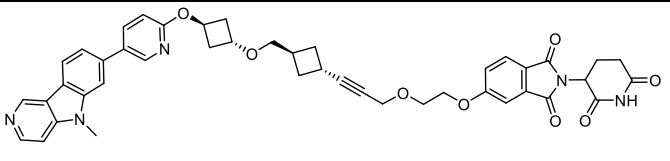
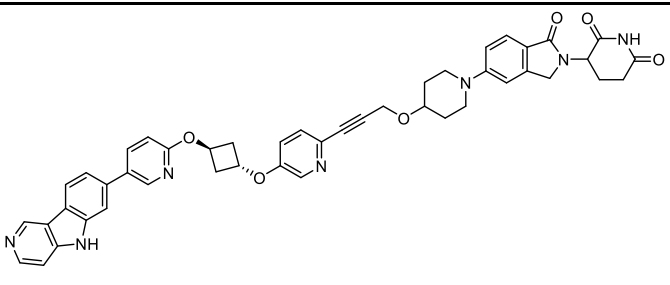
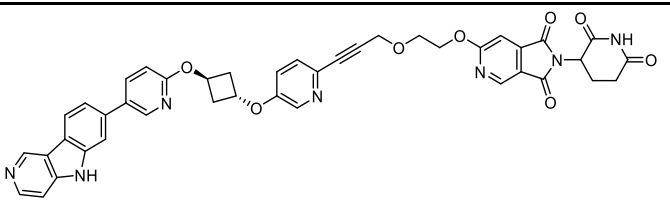
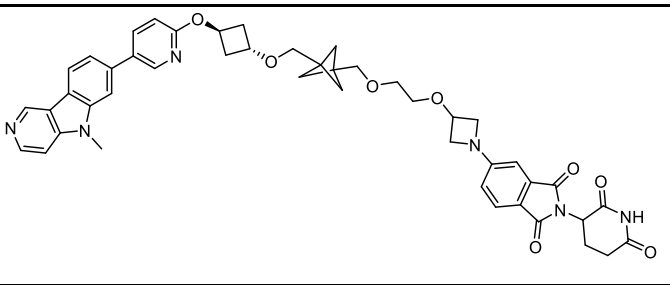
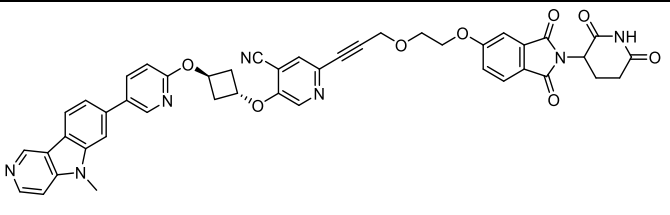
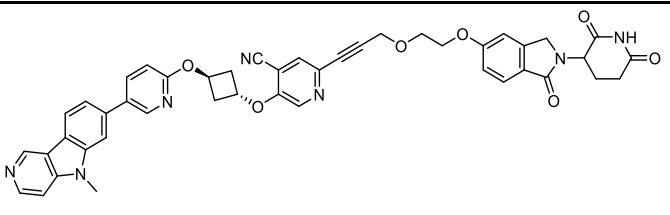
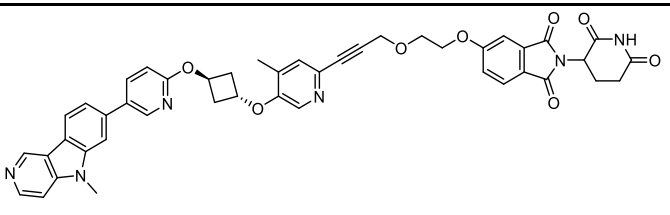
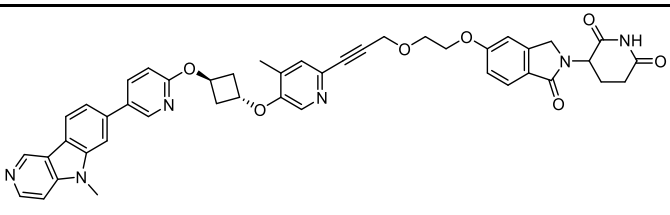
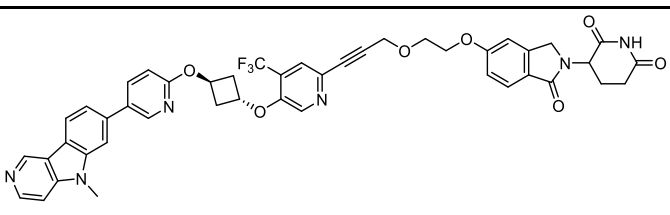
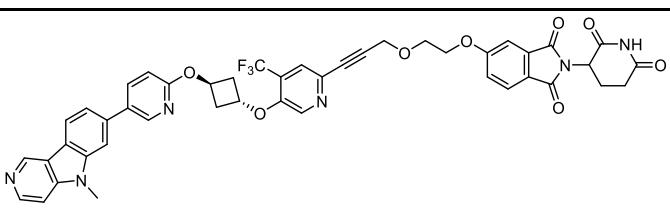
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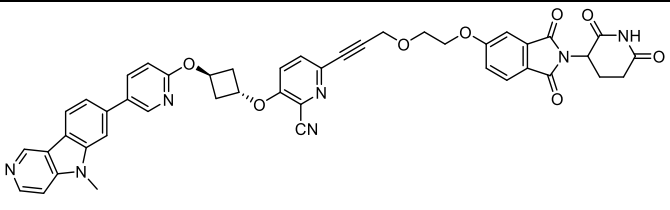
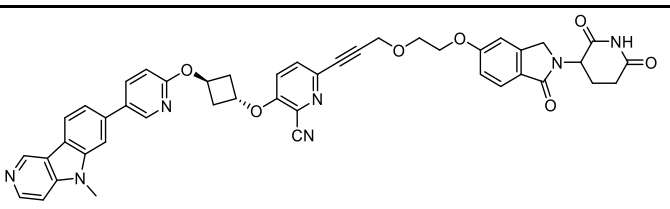
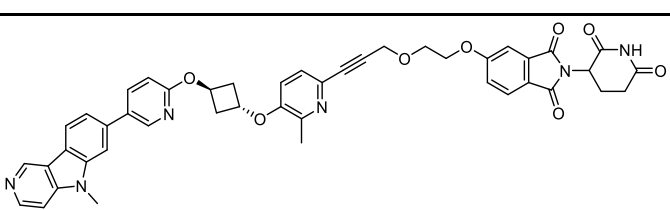
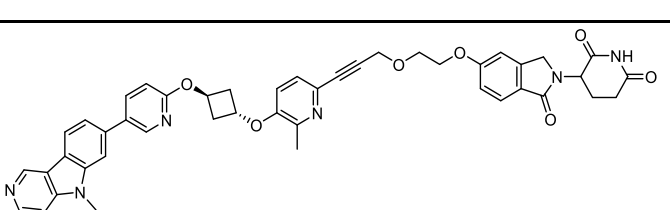
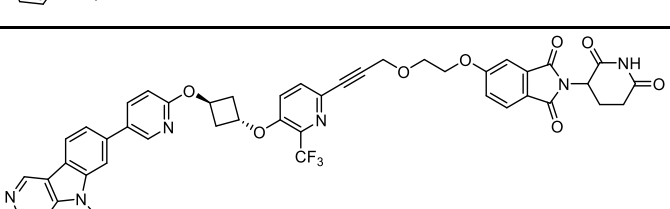
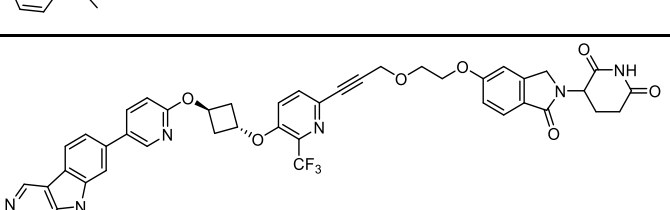
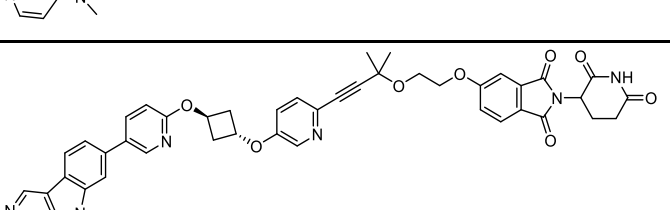
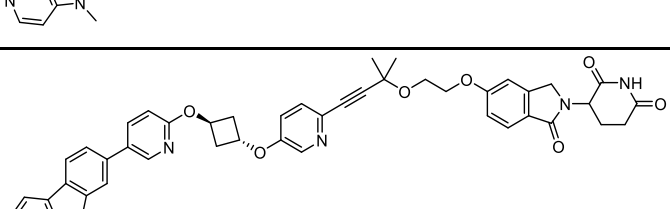
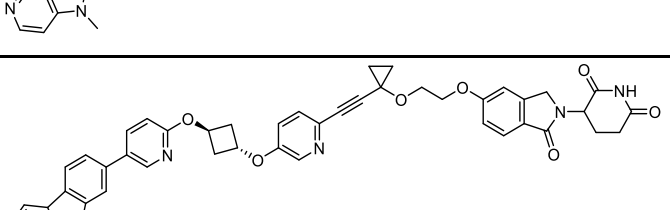
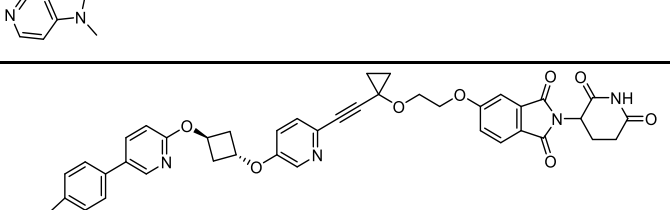
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| 249 |                                                                                                                          |  |  |  |
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| 251 |                                                                                                                          |  |  |  |
| 252 |                                                                                                                          |  |  |  |
| 253 | <br><chem>Cc1ccc2nc3ccccc3nc2c1-c1ccc(O[C@H]2C[C@@H](OCCN3CCCC3)OCCOCCOC4=CC(=O)c5ccccc5n4C6=CC(=O)NC(=O)CC6)=cn1</chem> |  |  |  |
| 254 | <br><chem>Cc1ccc2nc3ccccc3nc2c1-c1ccc(O[C@H]2C[C@@H](OCCN3CCCC3)OCCOCCOC4=CC(=O)c5ccccc5n4C6=CC(=O)NC(=O)CC6)=cn1</chem> |  |  |  |
| 255 | <br><chem>Cc1ccc2nc3ccccc3nc2c1-c1ccc(O[C@H]2C[C@@H](OCCN3CCCC3)OCCOCCOC4=CC(=O)c5ccccc5n4C6=CC(=O)NC(=O)CC6)=cn1</chem> |  |  |  |
| 256 | <br><chem>Cc1ccc2nc3ccccc3nc2c1-c1ccc(O[C@H]2C[C@@H](OCCN3CCCC3)OCCOCCOC4=CC(=O)c5ccccc5n4C6=CC(=O)NC(=O)CC6)=cn1</chem> |  |  |  |
| 257 | <br><chem>Cc1ccc2nc3ccccc3nc2c1-c1ccc(O[C@H]2C[C@@H](OCCN3CCCC3)OCCOCCOC4=CC(=O)c5ccccc5n4C6=CC(=O)NC(=O)CC6)=cn1</chem> |  |  |  |
| 258 | <br><chem>Cc1ccc2nc3ccccc3nc2c1-c1ccc(O[C@H]2C[C@@H](OCCN3CCCC3)OCCOCCOC4=CC(=O)c5ccccc5n4C6=CC(=O)NC(=O)CC6)=cn1</chem> |  |  |  |
| 259 | <br><chem>Cc1ccc2nc3ccccc3nc2c1-c1ccc(O[C@H]2C[C@@H](OCCN3CCCC3)OCCOCCOC4=CC(=O)c5ccccc5n4C6=CC(=O)NC(=O)CC6)=cn1</chem> |  |  |  |
| 260 | <br><chem>Cc1ccc2nc3ccccc3nc2c1-c1ccc(O[C@H]2C[C@@H](OCCN3CCCC3)OCCOCCOC4=CC(=O)c5ccccc5n4C6=CC(=O)NC(=O)CC6)=cn1</chem> |  |  |  |

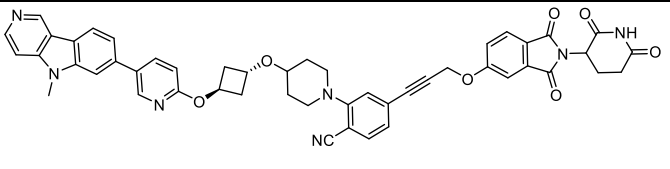
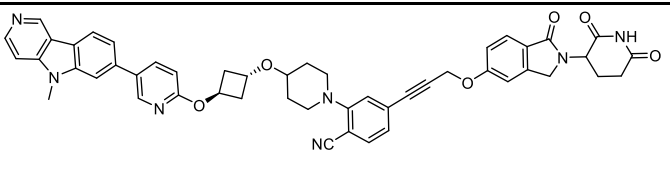
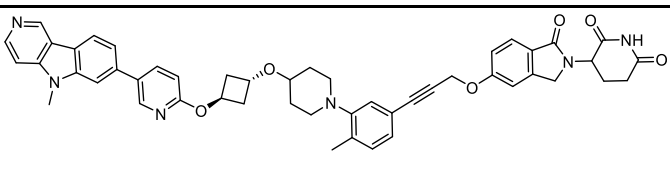
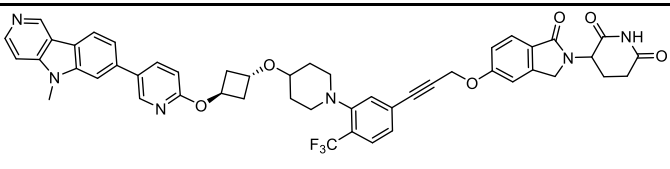
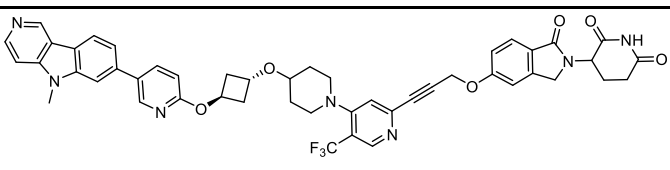
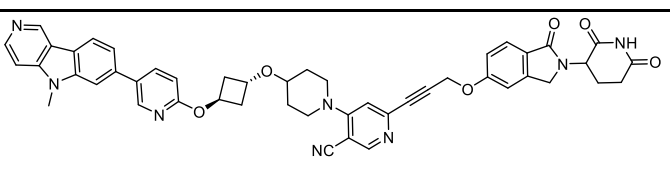
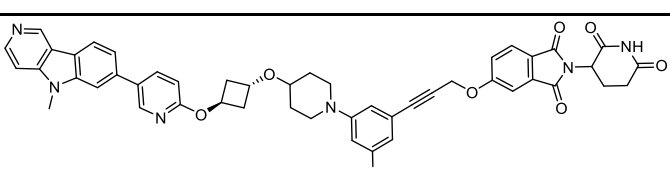
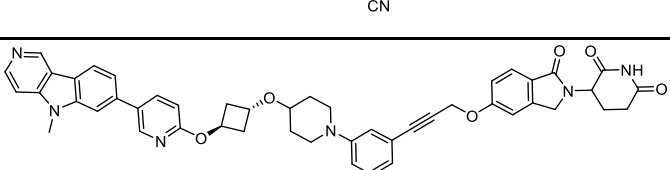
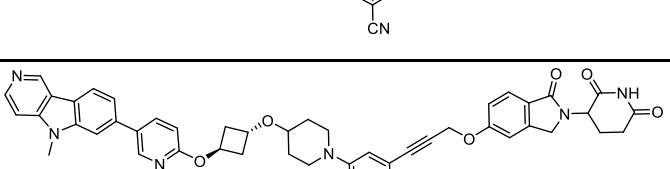
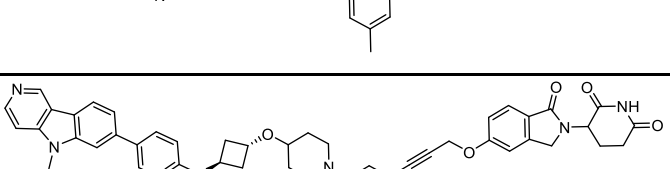
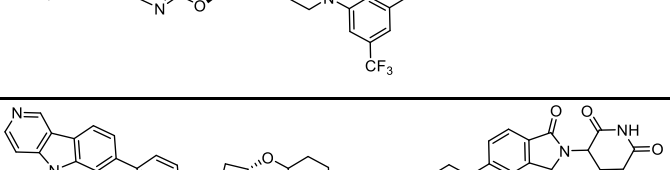
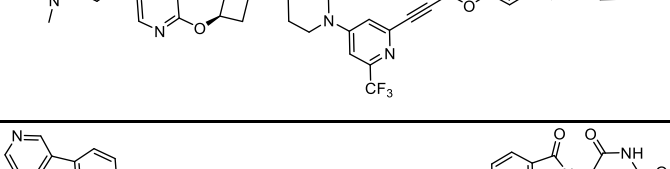
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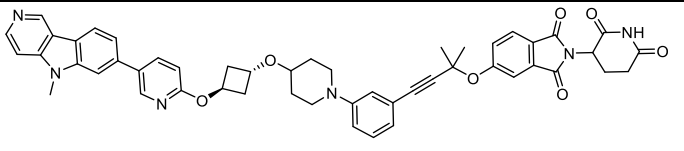
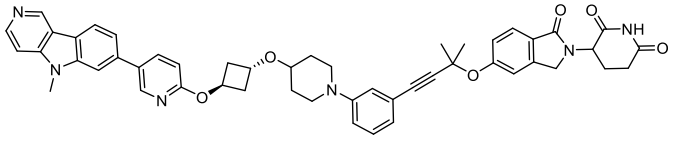
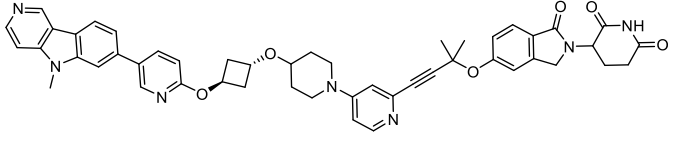
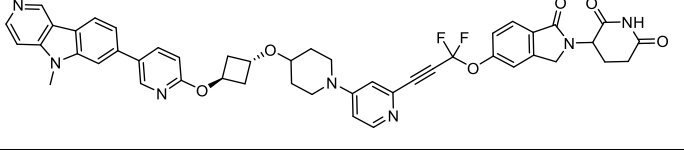
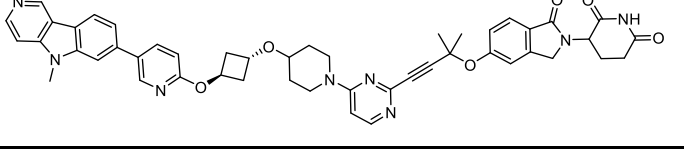
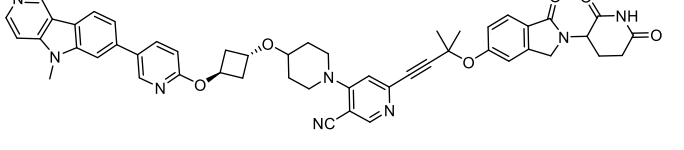
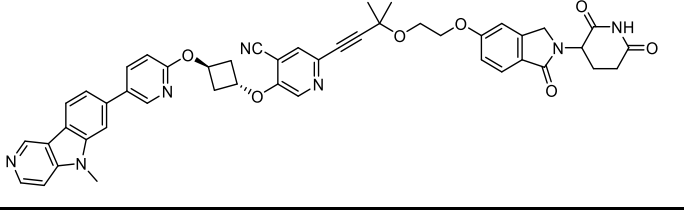
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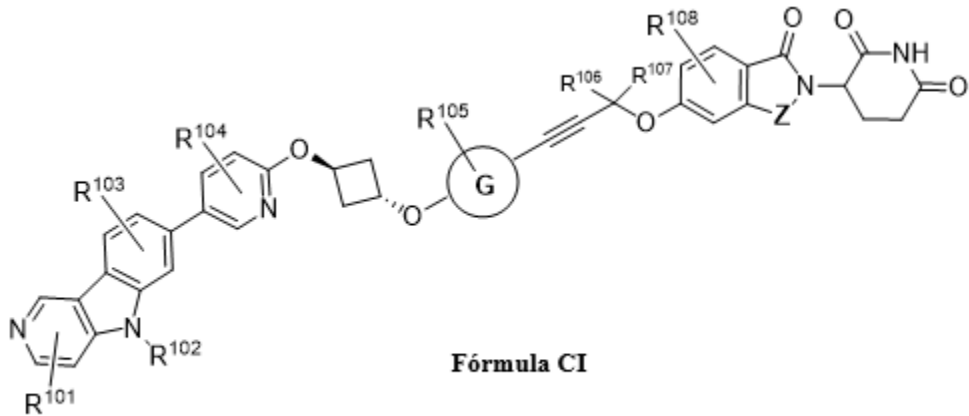
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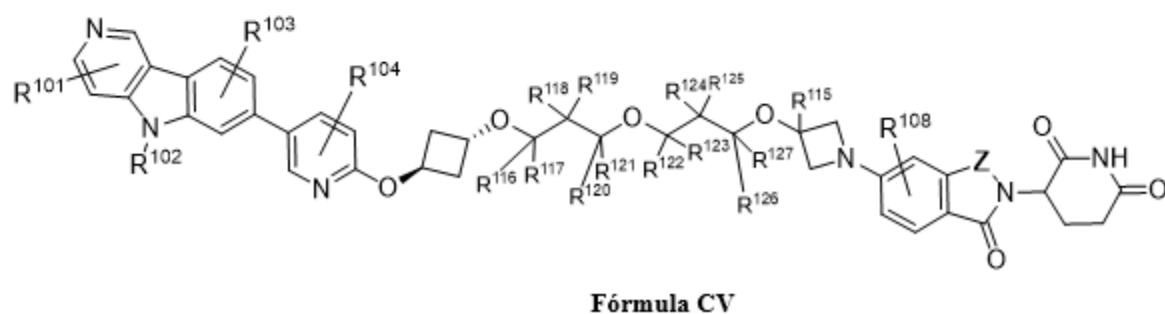
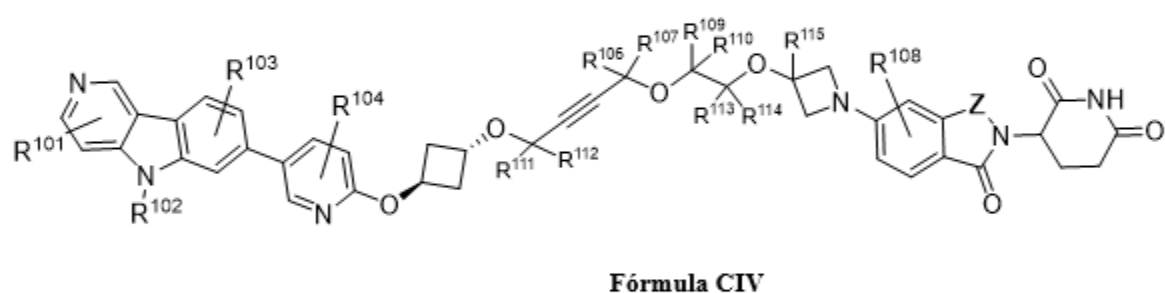
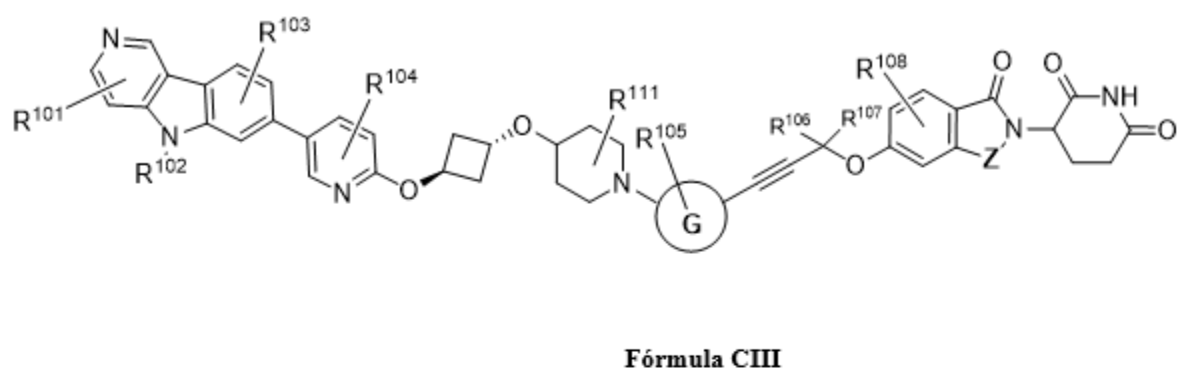
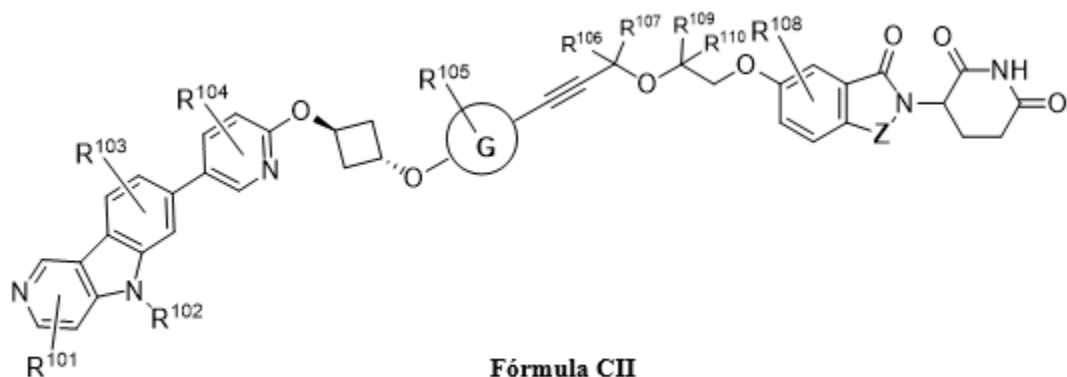
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13. El compuesto de conformidad con cualquiera de las reivindicaciones 1 a 12, en donde el compuesto tiene una estructura química seleccionada de las Fórmulas CI hasta CV:





en donde:

$R^{101}$  es 1–2 sustituyentes independientemente seleccionados de H, alquilo de  $C_{1-6}$ , halógeno, haloalquilo de  $C_{1-6}$  o ciano;

$R^{102}$  se selecciona de H, alquilo de  $C_{1-6}$ , o haloalquilo de  $C_{1-6}$ ;

$R^{103}$  es 1–2 sustituyentes independientemente seleccionados de H, alquilo de  $C_{1-6}$ , halógeno, haloalquilo de  $C_{1-6}$  o ciano;

$R^{104}$  es 1–2 sustituyentes independientemente seleccionados de H, alquilo de  $C_{1-6}$ , halógeno, haloalquilo de  $C_{1-6}$  o ciano;

$R^{105}$  es 1–2 sustituyentes independientemente seleccionados de H, alquilo de  $C_{1-6}$ , halógeno, haloalquilo de  $C_{1-6}$  o ciano;

$R^{106}$ ,  $R^{107}$ ,  $R^{109}$ ,  $R^{110}$ ,  $R^{111}$ ,  $R^{112}$ ,  $R^{113}$ ,  $R^{114}$ ,  $R^{116}$ ,  $R^{117}$ ,  $R^{120}$ ,  $R^{121}$ ,  $R^{126}$ ,  $R^{127}$ ,  $R^{122}$  y  $R^{123}$  se seleccionan cada uno independientemente de H, alquilo de  $C_{1-6}$ , halógeno o haloalquilo de  $C_{1-6}$ ;

$R^{108}$  es 1–2 sustituyentes independientemente seleccionados de H, halógeno, ciano o metoxi;

$R^{115}$  es H;

$R^{118}$  y  $R^{119}$  se seleccionan independientemente de H o halógeno, o  $R^{118}$  y  $R^{119}$  tomados juntos con el átomo de carbono al que se unen representan un anillo cicloalquilo o heterocicloalquilo de 3–6 miembros, tal como ciclopropano o un oxetano;

$R^{124}$  y  $R^{125}$  se seleccionan independientemente de H o halógeno, o  $R^{124}$  y  $R^{125}$  tomados juntos con el átomo de carbono al que se unen representan un anillo cicloalquilo o heterocicloalquilo de 3–6 miembros, tal como ciclopropano o un oxetano;

G es un fenilo o un anillo heteroarilo de 5 o 6 miembros; y

Z es  $CH_2$  o  $C=O$ .

14. Una composición que comprende un compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1 a 13, y un vehículo aceptable farmacéuticamente.