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Application No. 16 852 695.2 - 1111	Ref. EP117109FZ	Date 19.03.2020
Applicant Arrowhead Pharmaceuticals, Inc.		

Communication pursuant to Article 94(3) EPC

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(2) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

of 4 months

from the notification of this communication, this period being computed in accordance with Rules 126(2) and 131(2) and (4) EPC. One set of amendments to the description, claims and drawings is to be filed within the said period on separate sheets (R. 50(1) EPC).

If filing amendments, you must identify them and indicate the basis for them in the application as filed. Failure to meet either requirement may lead to a communication from the Examining Division requesting that you correct this deficiency (R. 137(4) EPC).

In case you withdraw the application within the above-mentioned period, the examination fee will be refunded at a rate of 50% (Art. 11 (b) RFees).

Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Art. 94(4) EPC).



Bucka, Alexander
Primary Examiner
For the Examining Division

Enclosure(s): 2 page/s reasons (Form 2906)

The examination is being carried out on the **following application documents**

Description, Pages

1-119 as published

Sequence listings, SEQ ID NO

1-1285 as published

Claims, Numbers

1-20 filed in electronic form on 02-03-2020

Drawings, Sheets

1-3 as published

- 1 The amendments of the claims submitted in electronic form on 2 March 2020 appear to be allowable in view of Article 123(2) EPC.
- 2 The present set of claims has been limited to the first invention, as defined in the European search opinion. The novelty (Article 54 EPC) of the claimed subject matter has been already acknowledged. The Applicant's comments submitted with the reply dated 2 March 2020 have been taken into account.
- 3 Claim 1 is directed to siRNA molecules targeting LPA comprising an antisense strand of SEQ ID NO: 1280, 1282, 1242, 1244, 1246 or 1254.

D1, the closest prior art, describes a siRNA targeting LPA, which differs from the nucleic acids of SEQ ID NO: 1280, etc. in its sequence. No effect is associated with this structural difference.

The problem to be solved is regarded to reside in the provision of further, alternative siRNA molecules targeting LPA, as apparently conceded by the Applicant.

The proposed solution, i. e. the specific siRNA molecules recited in claim 1, is considered to involve an inventive step within the meaning of Article 56 EPC.

In view of the disclosure of D1, which deals with an animal model of atherosclerosis, it was clearly desirable to identify siRNAs targeting the LPA transcript, e. g. for the treatment of cardiovascular diseases in humans. The same incentive could be derived from D3.

D1 refers to approaches to identify siRNA molecules that efficiently knockdown the rhesus monkey LPA transcript (cf. D1, page 47, left column), but does not suggest any particular region of the LPA transcript to be targeted. The two siRNAs, for which sequence information is provided (cf. D1, table 1), target a different sequence than the siRNAs recited in claim 1. In view of the unpredictability of obtaining functional siRNAs that are efficiently down-regulating a given target such as LPA, the skilled person would not have had a reasonable expectation to succeed in obtaining further siRNA molecules efficiently down-regulating LPA (some of the siRNAs encompassed by the scope of the claims are tested in example 15, figure 1, which relate to siRNAs comprising SEQ ID NO: 156, 164, 188). Neither D1 nor its combination with D2 or D3 would have led the skilled person in an obvious manner to the presently claimed subject matter. Thus, the subject matter of claims 1 to 20 meets the requirements of Article 56 EPC.

- 4 The Applicant is kindly asked to bring the description into conformity with the amended claims and the requirements of the EPC, in particular with the requirements of Article 82 EPC. The attention of the Applicant is drawn to the fact that the application may not be amended in such a way that it contains subject matter which extends beyond the content of the application as filed (Article 123(2) EPC). The Applicant is requested to indicate, where the basis of any amendment submitted can be found in the application as originally filed (Rule 137(4) EPC).

The Applicant is reminded of the provisions of Rule 137(3) EPC, which states that after amendments filed in reply to the first communication from the Examining Division, no further amendment may be made without the consent of the Examining Division.