**To:** ccmo_bi[bi@ccmo.nl]
**Cc:** [redacted]@qps.com]; [redacted]@qps.com]
**From:** [redacted]
**Sent:** Tue 7-1-2020 16:20:06
**Subject:** Digital submission of substantial amendment NL69548.056.19
**Received:** Tue 7-1-2020 16:20:10
A1a - Cover letter CCMO, dated 07 January 2020.pdf
B5 - EudraCT Substantial Amendment Form CCMO dated 07 January 2020.pdf
L1 - SUSAR report, RDN-929-103, dated 07 January 2020.pdf
L6 - Investigator Safety Letter (EU)_Initial, dated 06 January 2020.pdf

Dear members of the Central Committee on Research Involving Human Subjects/Minister of Health, Welfare and Sport,

With this letter QPS Netherlands B.V. sends the documents of the Rodin Therapeutics, Inc. study *"A two-part parallel group study to assess the safety, tolerability and pharmacokinetic (PK) profile of multiple oral doses of RDN-929 in healthy older adults and subjects with early symptomatic Alzheimer's Disease"* registered under NL69548.056.19.

The modification(s) of this amendment is/are concerning (please tick where appropriate):
*☐ htmlrtf the addition of a new investigational medicinal product;
*☐ htmlrtf a substantial modification of the current investigational medicinal product;
☒ otherwise, namely: Due to a third case of serum liver transaminase elevation the sponsor decided to put the study on hold. Please find the detailed rationale in the documents submitted as well as the SUSAR report for this case.

With this submission I declare that all relevant documents from the above-mentioned research dossier are signed by the authorised people. The signed documents are/will be submitted for review to the responsible review committee.

With Kind regards/Met vriendelijke groeten,

QPS
CUSTOM-BUILT RESEARCH™

[redacted]
QPS Netherlands BV | Petrus Campersingel 123 | 9713 AG Groningen | The Netherlands
Tel +31 50 368[redacted]
Email [redacted]@qps.com | Web www.qps.com

Please note that I am not in the office on Friday

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CUSTOM-BUILT RESEARCH™

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**Web** www.qps.com

**Bank** 5.1.2.e
**IBAN** 5.1.2.e
**BIC** 5.1.2.e
**Trade Registrar** 02083147
**VAT** NL812888601B01

Central Committee on Research Involving Human Subjects/Minister of Health, Welfare and Sport
PO Box 16302
2500 BH The Hague

Groningen, 07 January 2020

Subject: Digital submission of substantial amendment NL69548.056.19

Dear members of the Central Committee on Research Involving Human Subjects/Minister of Health, Welfare and Sport,

With this letter QPS Netherlands B.V. sends the documents of the Rodin Therapeutics, Inc. study *"A two-part parallel group study to assess the safety, tolerability and pharmacokinetic (PK) profile of multiple oral doses of RDN-929 in healthy older adults and subjects with early symptomatic Alzheimer's Disease"* registered under NL69548.056.19.

The modification(s) of this amendment is/are concerning (please tick where appropriate):
☐ the addition of a new investigational medicinal product;
☐ a substantial modification of the current investigational medicinal product;
☒ otherwise, namely: Due to a third case of serum liver transaminase elevation the sponsor decided to put the study on hold. Please find the detailed rationale in the documents submitted as well as the SUSAR report for this case.

With this submission I declare that all relevant documents from the above-mentioned research dossier are signed by the authorised people. The signed documents are/will be submitted for review to the responsible review committee.

Kind regards,

5.1.2.e

QPS Netherlands B.V.

**Substantial Amendment Notification Form (Cf. Section 3.7.b of the *Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial*[1])**

**NOTIFICATION OF A SUBSTANTIAL AMENDMENT TO A CLINICAL TRIAL ON A MEDICINAL PRODUCT FOR HUMAN USE TO THE COMPETENT AUTHORITIES AND FOR OPINION OF THE ETHICS COMMITTEES IN THE EUROPEAN UNION**

*For official use:*

| | |
|---|---|
| Date of receiving the request : | Grounds for non acceptance/ negative opinion : ☐<br>Date : |
| Date of start of procedure: | Authorisation/ positive opinion : ☐<br>Date : |
| Competent authority registration number of the trial:<br>Ethics committee registration number of the trial : | Withdrawal of amendment application ☐<br>Date : |

*To be filled in by the applicant:*

This form is to be used both for a request to the Competent Authority for authorisation of a **substantial** amendment and to an Ethics Committee for its opinion on a **substantial** amendment. Please indicate the relevant purpose in Section A.

## A TYPE OF NOTIFICATION

| | |
|---|---|
| **A.1 Member State in which the substantial amendment is being submitted:** | |
| **A.2Notification for authorisation to the competent authority:** | ☑ |
| **A.3Notification for an opinion to the ethics committee:** | ☐ |

## B TRIAL IDENTIFICATION *(When the amendment concerns more than one trial, repeat this form as necessary.)*

**B.1 Does the substantial amendment concern several trials involving the same IMP?**[2] yes ☐ no ☑

B.1.1 If yes repeat this section as necessary.

**B.2 Eudract number: 2019-000831-26**

**B.3 Full title of the trial** : A two-part parallel group study to assess the safety, tolerability and pharmacokinetic (PK) profile of multiple oral doses of RDN-929 in healthy older adults and subjects with early symptomatic Alzheimer's Disease

**B.4 Sponsor's protocol code number, version, and date:** Protocol RDN-929-103, amendment 2, 14 October 2019

## C IDENTIFICATION OF THE SPONSOR RESPONSIBLE FOR THE REQUEST

| **C.1** | **Sponsor** |
|---|---|
| C.1.1 | Organisation: Rodin Therapeutics, Inc. |
| C.1.2 | Name of person to contact: [redacted] |
| C.1.3 | Address : 852 Winter Street, Waltham, MA 02451, United States |
| C.1.4 | Telephone number : N/A |
| C.1.5 | Fax number : N/A |
| C.1.6 | e-mail: [redacted]@alkermes.com |

| **C.2** | **Legal representative[3] of the sponsor in the European Union for the purpose of this trial (if different from the sponsor)** |
|---|---|
| C.2.1 | Organisation: QPS Netherlands B.V. |
| C.2.2 | Name of person to contact: [redacted] |
| C.2.3 | Address : Petrus Campersingel 123, 9713 AG Groningen, The Netherlands |
| C.2.4 | Telephone number : +31 50 304 [redacted] |
| C.2.5 | Fax number : +31 50 304 [redacted] |
| C.2.6 | e-mail: N/A |

1 OJ, C82, 30.3.2010, p. 1; hereinafter referred to as 'detailed guidance CT-1'.

2 Cf. Section 3.7. of the detailed guidance CT-1.

3 As stated in Article 19 of Directive 2001/20/EC.

## D APPLICANT IDENTIFICATION (please tick the appropriate box)

| D.1 | Request for the competent authority | |
|---|---|---|
| D.1.1 | Sponsor | ☐ |
| D.1.2 | Legal representative of the sponsor | ☐ |
| D.1.3 | Person or organisation authorised by the sponsor to make the application. | ☑ |
| D.1.4 | Complete below: | |
| D.1.4.1 | Organisation : QPS Netherlands B.V. | |
| D.1.4.2 | Name of person to contact : 5.1.2.e [redacted] | |
| D.1.4.3 | Address : Petrus Campersingel 123, 9713 AG Groningen, The Netherlands | |
| D.1.4.4 | Telephone number : +31 50 304 5.1.2.e [redacted] | |
| D.1.4.5 | Fax number : +31 50 304 5.1.2.e [redacted] | |
| D.1.4.6 | E-mail: 5.1.2.e [redacted] @qps.com | |

| D.2 | Request for the Ethics Committee | |
|---|---|---|
| D.2.1 | Sponsor | ☐ |
| D.2.2 | Legal representative of the sponsor | ☐ |
| D.2.3 | Person or organisation authorised by the sponsor to make the application. | ☐ |
| D.2.4 | Investigator in charge of the application if applicable[4]: | |
| | • Co-ordinating investigator (for multicentre trial) | ☐ |
| | • Principal investigator (for single centre trial): | ☐ |
| D.2.5 | Complete below | |
| D.2.5.1 | Organisation : | |
| D.2.5.2 | Name : | |
| D.2.5.3 | Address : | |
| D.2.5.4 | Telephone number : | |
| D.2.5.5 | Fax number : | |
| D.2.6 | E-mail : | |

## E SUBSTANTIAL AMENDMENT IDENTIFICATION

**E.1 Sponsor's substantial amendment code number, version, date for the clinical trial concerned:**
(Protocol RDN-929-103, amendment 2, 14 October 2019)

| E.2 | Type of substantial amendment | |
|---|---|---|
| E.2.1 | **Amendment to information in the CT application form** | yes ☐ no ☑ |
| E.2.2 | **Amendment to the protocol** | yes ☐ no ☑ |
| E.2.3 | **Amendment to other documents appended to the initial application form** | yes ☐ no ☑ |
| E.2.3.1 | If yes specify: | |
| E.2.4 | **Amendment to other documents or information:** | yes ☐ no ☑ |
| E.2.4.1 | If yes specify: | |
| E.2.5 | **This amendment concerns mainly urgent safety measures already implemented[5]** | yes ☐ no ☑ |
| E.2.6 | **This amendment is to notify a temporary halt of the trial[6]** | yes ☑ no ☐ |
| E.2.7 | **This amendment is to request the restart of the trial[7]** | yes ☐ no ☑ |

4 According to national legislation.
5 Cf. Section 3.9. of the detailed guidance CT-1.
6 Cf. Section 3.10. of the detailed guidance CT-1.
7 Cf. Section 3.10. of the detailed guidance CT-1.

| E.3 | Reasons for the substantial amendment: | |
|---|---|---|
| E.3.1 | **Changes in safety or integrity of trial subjects** | **yes** ☑ **no** ☐ |
| E.3.2 | **Changes in interpretation of scientific documents/value of the trial** | **yes** ☐ **no** ☑ |
| E.3.3 | **Changes in quality of IMP(s)** | **yes** ☐ **no** ☑ |
| E.3.4 | **Changes in conduct or management of the trial** | yes ☐ no ☑ |
| E.3.5 | **Change or addition of principal investigator(s), co-ordinating investigator** | **yes** ☐ **no** ☑ |
| E.3.6 | **Change/addition of site(s)** | **yes** ☐ **no** ☑ |
| E.3.7 | **Other change** | **yes** ☐ **no** ☑ |
| E.3.7.1 | **If yes, specify:** | |
| E.3.8 | **Other case** | **yes** ☐ **no** ☑ |
| E.3.8.1 | **If yes, specify** | |

| E.4 | Information on temporary halt of trial[8] | |
|---|---|---|
| E.4.1 | **Date of temporary halt** (YYYY/MM/DD) **2019/12/26** | |
| E.4.2 | **Recruitment has been stopped** | yes ☑ no ☐ |
| E.4.3 | **Treatment has been stopped** | yes ☑ no ☐ |
| E.4.4 | Number of patients still receiving treatment at time of the temporary halt in the MS concerned by the amendment 2 | |
| E.4.5 | **Briefly describe (free text)**: | |

- Justification for a temporary halt of the trial
- The proposed management of patients receiving treatment at time of the halt *(free text).*

During the study to date, three subjects have experienced serum liver transaminase (alanine transaminase and aspartate transaminase) elevations above two times the upper limit of normal. Two of the subjects were included in Part 1 of the study, received the 200 mg dose level of RDN-929, and demonstrated returns to normal levels of serum transaminases off of study drug. The third subject was in Part 2 of the study, received the 50 mg dose level of RDN-929, and is still being monitored with repeat laboratory testing off study drug. After the third subject with elevated serum transaminases above two times the upper limit of normal, the decision was made to halt further dosing of ongoing subjects as well as recruitment while an evaluation of the third case of elevated serum transaminases could be conducted. The two remaining ongoing subjects in the study were informed to stop taking study drug on December 26, 2019 and to return to the clinic for an Early Termination visit followed by an End of Study visit approximately one week later. Laboratory testing, including serum transaminases, will be conducted per protocol for these two subjects at the Early Termination and End of Study visits. These subjects will not be required to complete the CSF sampling or PET scan assessments, however, given the short duration of exposure to study drug.

## F DESCRIPTION OF EACH SUBSTANTIAL AMENDMENT[9] *(free text)*:

| Previous and new wording in track change modus | New wording | Comments/explanation/reasons for substantial amendment |
|---|---|---|
| | | Please refer to section E4 |

## G CHANGE OF CLINICAL TRIAL SITE(S)/INVESTIGATOR(S) IN THE MEMBER STATE CONCERNED BY THIS AMENDMENT

| G.1 | Type of change |
|---|---|

[8] Cf. Section 3.10. of the detailed guidance CT-1.

[9] Cf. Section 3.7.c. of the detailed guidance CT-1. The sponsor may submit this documentation on a separate sheet.

G.1.1 **Addition of a new site**
G.1.1.1 **Principal investigator** (provide details below)
G.1.1.1.1 Given name
G.1.1.1.2 Middle name (if applicable)
G.1.1.1.3 Family name
G.1.1.1.4 Qualifications (MD……..)
G.1.1.1.5 Professional address
G.1.2 **Removal of an existing site**
G.1.2.1 **Principal investigator** (provide details below)
G.1.2.1.1 Given name
G.1.2.1.2 Middle name (if applicable)
G.1.2.1.3 Family name
G.1.2.1.4 Qualifications (MD……..)
G.1.2.1.5 Professional address
G.1.3 **Change of co-ordinating investigator** (provide details below of the new coordinating investigator)
G.1.3.1 Given name
G.1.3.2 Middle name
G.1.3.3 Family name
G.1.3.4 Qualification (MD……)
G.1.3.5 Professional address
G.1.3.6 Indicate the name of the previous co-ordinating investigator:
G.1.4 **Change of principal investigator at an existing site** (provide details below of the new principal investigator)
G.1.4.1 Given name
G.1.4.2 Middle name
G.1.4.3 Family name
G.1.4.4 Qualifications (MD……..)
G.1.4.5 Professional address
G.1.4.6 Indicate the name of the previous principal investigator:

## H CHANGE OF INSTRUCTIONS TO CA FOR FEEDBACK TO SPONSOR

| | |
|---|---|
| **H.1 Change of e-mail contact for feedback on application*** | |
| **H.2** Change to request to receive an .xml copy of CTA data | ☐ yes ☑ no |
| H.2.1 Do you want a .xml file copy of the CTA form data saved on EudraCT? | ☐ yes ☑ no |
| H.2.1.1 If yes provide the e-mail address(es) to which it should be sent (up to 5 addresses): | |
| H.2.2 Do you want to receive this via password protected link(s)[10]? | ☐ yes ☑ no |
| If you answer no to question H.2.2 the .xml file will be transmitted by less secure e-mail link(s) | |
| H.2.3 Do you want to stop messages to an email for which they were previously requested? | ☐ yes ☑ no |
| H.2.3.1 If yes provide the e-mail address(es) to which feedback should no longer be sent: | |
| **(*This will only come into effect from the time at which the request is processed in EudraCT).** | |

## I LIST OF THE DOCUMENTS APPENDED TO THE NOTIFICATION FORM (cf. Section 3.7 of detailed guidance CT-1)

*Please submit only relevant documents and/or when applicable make clear references to the ones already submitted. Make clear references to any changes of separate pages and submit old and new texts. Tick the appropriate box(es).*

| | |
|---|---|
| **I.1 Cover letter** | ☑ |
| **I.2 Extract from the amended document in accordance with Section 3.7.c. of detailed guidance CT-1 (if not contained in Part F of this form)** | ☐ |
| **I.3 Entire new version of the document[11]** | ☐ |

[10] This requires a EudraLink account. (See https://eudract.ema.europa.eu/ for details)

| | |
|---|---|
| **I.4 Supporting information** | ☐ |
| **I.5 Revised .xml file and copy of initial application form with amended data highlighted** | ☐ |
| **I.6 Comments on any novel aspect of the amendment if any :** | |

## J SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

**J.1** I hereby confirm that/ confirm on behalf of the sponsor that (delete which is not applicable)

- The above information given on this request is correct;
- The trial will be conducted according to the protocol, national regulation and the principles of good clinical practice; and
- It is reasonable for the proposed amendment to be undertaken.

| **J.2** ☑ | **APPLICANT OF THE REQUEST FOR THE COMPETENT AUTHORITY**(as stated in section D.1): |
|---|---|
| J.2.1 | Signature [redacted] 5.1.2.e |
| J.2.2 | Print nam[redacted] |
| J.2.3 | Date : 07 January 2020 |

| **J.3** | **APPLICANT OF THE REQUEST FOR THE ETHICS COMMITTEE** (as stated in section D.2): ☑ 5.1.2.e 07 Jan '20 |
|---|---|
| J.3.1 | Signature [13]: |
| J.3.2 | Print name: |
| J.3.3 | Date : |

[11] Cf. Section 3.7 c. of the detailed guidance CT-1.

[12] On an application to the Competent Authority only, the applicant to the Competent Authority needs to sign.

[13] On an application to the Ethics Committee only, the applicant to the Ethics Committee needs to sign.

# SUSPECT ADVERSE REACTION REPORT

EUDRACT Number: 2019-000831-26

## I. REACTION INFORMATION

| 1. PATIENT INITIALS (first, last) | 1a. COUNTRY | 2. DATE OF BIRTH | | | 2a. AGE | 3. SEX | 3a. WEIGHT | 4-6 REACTION ONSET | | | 8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day | Month | | | | | Day | Month | Year | |
| 5.1.2.e | 5.1.2.e | | | 5.1.2.e | 5.1.2.e | 5.1.2.e | 5.1.1.d | 23 | DEC | 2019 | |

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

5.1.1.d ]

Case Description:

5.1.1.d

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

## II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1 ) RDN-929 (RDN-929) Capsule

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1 ) 50 milligram, qd

16. ROUTE(S) OF ADMINISTRATION
#1 ) Oral

17. INDICATION(S) FOR USE
#1 ) Dementia Alzheimer's type (Dementia Alzheimer's type)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1 ) 20-NOV-2019 / 17-DEC-2019

19. THERAPY DURATION
#1 ) 27 days

## III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

| From/To Dates | Type of History / Notes | Description |
|---|---|---|
| 5.1.1.d | 5.1.1.d | 5.1.1.d |

## IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Rodin Therapeutics, Inc.
852 Winter Street
Waltham, MA 02451 UNITED STATES
Phone: +1 5.1.1.e

26. REMARKS
Patient ID: 5.1.2.e
Study ID: RDN-929-103
Center ID: 5.1.2.e

24b. MFR CONTROL NO.
5.1.1.c

25b. NAME AND ADDRESS OF REPORTER
5.1.2.e

24c. DATE RECEIVED BY MANUFACTURER
24-DEC-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
07-JAN-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 5.1.1.c

## ADDITIONAL INFORMATION

**7+13. DESCRIBE REACTION(S) continued**

Study sponsor determined the event to be serious based on medical importance on 24-DEC-2019. SAE reports with initial and follow-up information was received on 03-JAN-2020 and 06-JAN-2020.

Medical history included 5.1.1.d

5.1.1.d

5.1.1.d

5.1.1.d

5.1.1.d

5.1.1.d

5.1.1.d

5.1.1.d

5.1.1.d

5.1.1.d

5.1.1.d

5.1.1.d

As of 02-JAN-2020, approximately 86 healthy subjects and 7 subjects with early symptomatic Alzheimer's disease (AD) have been exposed to RDN-929. Of all subjects exposed to RDN-929,

5.1.1.d

5.1.1.d

**13. Lab Data**

| # | Date | Test / Assessment / Notes | Results | Normal High / Low |
|---|---|---|---|---|
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |

Mfr. Control Number: 5.1.1.c

## ADDITIONAL INFORMATION

**13. Lab Data**

| # | Date | Test / Assessment / Notes | Results | Normal High / Low |
|---|---|---|---|---|
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d | 5.1.1.d |

**13. Relevant Tests**

5.1.1.d

07-Jan-2020 02:33

Mfr. Control Number: 5.1.1.c

## ADDITIONAL INFORMATION

**13. Relevant Tests**




5.1.1.d

**23. OTHER RELEVANT HISTORY continued**

| From/To Dates | Type of History / Notes | Description |
|---|---|---|
| 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d<br>5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d | 5.1.1.d |
| 5.1.1.d | 5.1.1.d<br>5.1.1.d | 5.1.1.d |

Rodin Therapeutics
852 Winter Street
Waltham, MA 02451
United States
+1 5.1.2.e
https://www.alkermes.com

06JAN2020

RE: SUSAR for filing with Rodin Therapeutics (entity of Alkermes, Inc.) IMP: RDN-929;
Case ID: 5.1.1.c
Study ID: RDN-929-103;
EudraCT Number: 2019-000831-26

Dear Investigator,

In accordance with Directive 2001/20/EC of the European Parliament, and of the Council of 4 April 2001, Article 18, sponsors of clinical drug studies conducted in the European Union (EU) must notify all participating investigators, Ethics Committees and competent authorities of any reports of suspected adverse reactions to the drug under study that are both unexpected and serious. These suspected adverse reaction reports may come from an investigational study, marketed use of a drug, or the published literature and may include patient populations different to those included in the study you are participating in.

The reporting of this information does not necessarily reflect a conclusion by the sponsor that the drug/investigational medicinal product (IMP) caused or contributed to the reported adverse reaction(s). If it is later determined the study drug caused the adverse event, the Investigator's Brochure will be updated as appropriate and communicated to you separately.

Please retain a copy of the written safety report as well as documentation of the submission of this report, as appropriate, to your Independent Ethics Committee (IEC) in your study files.

Please note that, consistent with the confidentiality provisions of your clinical study agreement, this letter and the attached report(s) may not be disclosed to any person other than your IEC and must be kept confidential by you and by your IEC.

Please contact your study monitor with any additional questions and/or concerns you may have.

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Sincerely,

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