To: ccmo_bi[bi@ccmo.nl]
Cc: [redacted]@qps.com]
From: [redacted]
Sent: Mon 14-10-2019 15:03:24
Subject: Digital submission of substantial amendment NL69548.056.19
Received: Mon 14-10-2019 15:03:29
B3 - EudraCT application form CCMO, 14 April 2019.pdf
B5 - EudraCT Substantial Amendment Form CA, 14 October 2019.pdf
A1 - Cover letter applicant CCMO, dated 14 October 2019.pdf

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

With this letter I would like to ask the Competent Authority (Central Committee on Research Involving Human Subjects/Minister of Health, Welfare and Sport) to issue a certificate of no objection for a substantial amendment belonging to the research entitled "*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):
*騑htmlrtf the addition of a new investigational medicinal product;
*騑htmlrtf a substantial modification of the current investigational medicinal product;
*醆htmlrtf otherwise, namely: With this amendment, the address of the sponsor was updated, the dosage level of Part 2 was set at 50 mg, the exclusion criterion regarding liver values at Screening was updated, the fasting requirement before clinical laboratory tests was updated, and a fasting requirement before PET scanning was added. Furthermore, sections describing stopping rules when liver values are increased 2x above ULN, describing additional one time hepatic assessments and describing study stopping rule were added.

With this submission I declare that all relevant documents from the above-mentioned research dossier are signed by the authorized people. The signed documents are/will be submitted for review to the responsible review commit-tee specified in question I1 of the general assessment and registration form (ABR form).

With Kind regards/Met vriendelijke groeten,

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

Annex 1: Clinical trial Application Form

REQUEST FOR AUTHORISATION OF A CLINICAL TRIAL ON A MEDICINAL PRODUCT FOR HUMAN USE TO THE COMPETENT AUTHORITIES AND FOR OPINION OF THE ETHICS COMMITTEES IN THE COMMUNITY

To be filled in by the applicant
The questions in this form for the request for authorisation from the Competent Authority are also relevant for the opinion from an Ethics Committee (it represents module 1 of the form for applying to an ethics committee) and can be used as part of that application. Please indicate the relevant purpose in a box below.

REQUEST FOR AUTHORISATION TO THE COMPETENT AUTHORITY: **Yes ●**
REQUEST FOR OPINION OF THE ETHICS COMMITTEE: **No ●**

A. TRIAL IDENTIFICATION

A.1	Member State in which the submission is being made:	**Netherlands - Competent Authority**
A.2	EudraCT number:	**2019-000831-26**
A.3	Full title of the trial:	
	English	**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**
A.3.1	Title of the trial for lay people, in easily understood, i.e. non-technical, language:	
	English	**To assess the safety, tolerability, uptake and breakdown of multiple doses RDN-929 in healthy older adults and in adults with early symptomatic Alzheimer's Disease**
A.3.2	Name or abbreviated title of the trial where available:	
A.4	Sponsor's protocol code number, version and date[1]:	
A.4.1	Sponsor's protocol code number:	**RDN-929-103**
A.4.2	Sponsor's protocol version:	**amendmt 2**
A.4.3	Sponsor's protocol date:	**2019-10-11**
A.5	Additional international study identifiers (e.g. WHO, ISRCTN[2] , US NCT Number[3]) if available	
A.5.1	ISRCTN number:	
A.5.2	US NCT number:	
A.5.3	WHO Universal Trial Number (UTN):	
A.5.4	Other Identifier:	
A.6	Is this a resubmission?	**No ●**
	If 'Yes', indicate the resubmission letter[4]: **First Submission**	
A.7	Is the trial part of an agreed Paediatric Investigation Plan?	**No ●**
A.8	EMA Decision number of Paediatric Investigation Plan:	

B. IDENTIFICATION OF THE SPONSOR RESPONSIBLE FOR THE REQUEST

B.1	SPONSOR	
B.1.1	Name of organisation:	**Rodin Therapeutics, Inc.**
B.1.2	Name of the person to contact:	
B.1.2.1	Given name	[redacted]
B.1.2.2	Middle name	
B.1.2.3	Family name	[redacted]
B.1.3	Address:	
B.1.3.1	Street address	**300 Technology Square, 8th Floor**
B.1.3.2	Town/city	**Cambridge**
B.1.3.3	Post code	**MA02139**
B.1.3.4	Country	**United States**
B.1.4	Telephone number:	**+1** [redacted]
B.1.5	Fax number:	
B.1.6	E-mail:	[redacted]**@rodintherapeutics.com**

B.2	LEGAL REPRESENTATIVE [5] OF THE SPONSOR IN THE COMMUNITY FOR THE PURPOSE OF THIS TRIAL (if different from the sponsor)	
B.2.1	Name of organisation:	**QPS Netherlands B.V.**
B.2.2	Name of person to contact:	
B.2.2.1	Given name	[redacted]
B.2.2.2	Middle name	
B.2.2.3	Family name	[redacted]
B.2.3	Address:	
B.2.3.1	Street address	**Petrus Campersingel 123**
B.2.3.2	Town/city	**Groningen**
B.2.3.3	Post code	**9713AG**
B.2.3.4	Country	**Netherlands**
B.2.4	Telephone number:	**+31 50 304**[redacted]
B.2.5	Fax number:	**+31 50 304**[redacted]
B.2.6	E-mail:	

B.3	STATUS OF THE SPONSOR:	
B.3.1	Commercial:	**Yes •**
B.3.2	Non commercial:	**No •**

B.4	Source(s) of Monetary or Material Support for the clinical trial (repeat as necessary):	
B.4.1	Name of organisation:	**Rodin Therapeutics, Inc.**
B.4.2	Country:	**United States**

B.5	Contact point [6] designated by the sponsor for further information on the trial	
B.5.1	Name of organisation:	**Rodin Therapeutics, Inc.**
B.5.2	Functional name of contact point (e.g. "Clinical Trial Information Desk"):	[redacted]
B.5.3	Address:	
B.5.3.1	Street address	**300 Technology Square, 8th Floor**
B.5.3.2	Town/city	**Cambridge**
B.5.3.3	Post code	**MA02139**
B.5.3.4	Country	**United States**
B.5.4	Telephone number:	**+1** [redacted]
B.5.5	Fax number:	
B.5.6	E-mail: (use a functional e-mail address rather than a personal one)	[redacted]**@rodintherapeutics.com**

C. APPLICANT IDENTIFICATION, (please tick the appropriate box)

C.1	**REQUEST FOR THE COMPETENT AUTHORITY**		
C.1.1	Sponsor		
C.1.2	Legal representative of the sponsor		
C.1.3	Person or organisation authorised by the sponsor to make the application		**Yes •**
C.1.4	Complete the details of the applicant below even if they are provided elsewhere on the form:		
C.1.4.1	Name of Organisation:	**QPS Netherlands B.V.**	
C.1.4.2	Name of contact person:		
C.1.4.2.1	Given name	[redacted]	
C.1.4.2.2	Middle name		
C.1.4.2.3	Family name	[redacted]	
C.1.4.3	Address:		
C.1.4.3.1	Street address	**Petrus Campersingel 123**	
C.1.4.3.2	Town/city	**Groningen**	
C.1.4.3.3	Post code	**9713 AG**	
C.1.4.3.4	Country	**Netherlands**	
C.1.4.4	Telephone number:	**+31 50 304**[redacted]	
C.1.4.5	Fax number:	**+31 50 304**[redacted]	
C.1.4.6	E-mail:	[redacted]**@qps.com**	
C.1.5	Request to receive a copy of CTA data as XML:		
C.1.5.1	Do you want a copy of the CTA form data saved on EudraCT as an XML file?		**No •**
C.1.5.1.1	If Yes provide the e-mail address(es) to which it should be sent (up to 5 addresses):		
C.1.5.1.2	Do you want to receive this via password protected link(s)[7]?		**No •**
If you answer No to question C.1.5.1.2 the .xml file will be transmitted by less secure e-mail link(s)			

D. INFORMATION ON EACH IMP

Information on each 'bulk product' before trial-specific operations (blinding, trial specific packaging and labelling) should be provided in this section for each investigational medicinal product (IMP) being tested including each comparator and each placebo, if applicable. ***For placebo go directly to D.8****. If the trial is performed with several products use extra pages and give each product a sequential number in D.1.1. If the product is a combination product, information should be given for each active substance.*

D.1	**IMP IDENTIFICATION**	
Indicate which of the following is described below, then repeat as necessary for each of the numbered IMPs to be used in the trial (assign numbers from 1-n):		
D.1.1	This refers to the IMP number:	**PR1**
D.1.2	IMP being tested	**Yes ●**
D.1.3	IMP used as a comparator	**No ●**

D.2	**STATUS OF THE IMP**	
D.2.1	Has the IMP to be used in the trial a marketing authorisation?	**No ●**
If the IMP has a marketing authorisation in the Member State concerned by this application, but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2.		
D.2.1.1	If 'Yes', specify the product to be used in the clinical trial:	
D.2.1.1.1	Trade name	
D.2.1.1.1.1	EV Product Code (where applicable)	
D.2.1.1.2	Name of the Marketing Authorisation Holder:	
D.2.1.1.3	Marketing Authorisation number (if Marketing Authorisation granted by a Member State):	
D.2.1.1.4	Is the IMP modified in relation to its Marketing Authorisation?	**No ●**
D.2.1.1.4.1	If 'Yes', please specify:	
D.2.1.2	The country that granted the Marketing Authorisation	
D.2.1.2.1	Is this the Member State concerned with this application?	**No ●**

D.2.2	Situations where an IMP to be used in the CT has a Marketing Authorisation in the Member State concerned, but the protocol allows that any brand of the IMP with a Marketing Authorisation in that Member State be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start	
D.2.2.1	In the protocol, is treatment defined only by active substance?	**No ●**
D.2.2.1.1	If 'Yes', give active substance in D.3.8 or D.3.9	
D.2.2.2	In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?	**No ●**
D.2.2.2.1	If 'Yes', give active substance in D.3.8 or D.3.9	
D.2.2.3	The products to be administered as IMPs are defined as belonging to an ATC group[9]	**No ●**
D.2.2.3.1	If 'Yes', give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.3	
D.2.2.4	Other:	**No ●**
D.2.2.4.1	If 'Yes', please specify:	

D.2.3	IMPD submitted:	
D.2.3.1	Full IMPD:	**Yes ●**
D.2.3.2	Simplified IMPD:	**No ●**
D.2.3.3	Summary of product characteristics (SmPC) only:	**No ●**
D.2.4	Has the use of the IMP been previously authorised in a	**No ●**

	clinical trial conducted by the sponsor in the Community?	
D.2.4.1	If 'Yes' specify which Member States:	

D.2.5	Has the IMP been designated in this indication as an orphan drug in the Community?	**No ●**
D.2.5.1	If 'Yes', give the orphan drug designation number[10]:	

D.2.6	Has the IMP been the subject of scientific advice related to this clinical trial?	**No ●**
D.2.6.1	If 'Yes' to D.2.6, please indicate source of advice and provide a copy in the CTA request:	
D.2.6.1.1	CHMP[11]?	**No ●**
D.2.6.1.2	National Competent Authority?	**No ●**

D.3	**DESCRIPTION OF THE IMP**	
D.3.1	Product name where applicable[12]:	
D.3.2	Product code where applicable[13]:	**RDN-929**
D.3.3	ATC codes, if officially registered[14]:	
D.3.4	Pharmaceutical form (use standard terms):	**Capsule**
D.3.4.1	Is this a specific paediatric formulation?	**No ●**
D.3.5	Maximum duration of treatment of a subject according to the protocol: **once daily for 28 days**	
D.3.6	Dose allowed:	
D.3.6.1	For first trial only:	
	Specify per day or total	**Not Answered ●**
	Specify total dose (number and unit):	
	Route of administration (relevant to the first dose):	
D.3.6.2	For all trials	
	Specify per day or total	**Total ●**
	Specify total dose (number and unit):	**200 mg milligram(s)**
	Route of administration (relevant to the maximum dose):	**Oral use**
D.3.7	Routes of administration (use standard terms):	**Oral use**

D.3.8	Name of each active substance (INN or proposed INN if available): **N.Ap.**	
D.3.9	Other available name for each active substance (provide all available):	
D.3.9.1	CAS[15] number	**N.Ap.**
D.3.9.2	Current sponsor code	**RDN-929**
D.3.9.3	Other descriptive name **RDN-929 MALATE**	
D.3.9.4	EV Substance code	**SUB193800**
D.3.9.5	Full Molecular formula **C21H19F2N502**	
D.3.9.6	Chemical/biological description of the Active Substance	
D.3.10	Strength (specify all strengths to be used):	
D.3.10.1	Concentration unit:	**mg milligram(s)**
D.3.10.2	Concentration type ("exact number", "range", "more than" or "up to"):	**not less then**
D.3.10.3	Concentration (number).	**25**

D.3.11	Type of IMP	
Does the IMP contain an active substance:		
D.3.11.1	Of chemical origin?	**Yes ●**
D.3.11.2	Of biological / biotechnological origin (other than Advanced Therapy IMP (ATIMP)?	**No ●**
Is this a:		

D.3.11.3	Advanced Therapy IMP (ATIMP)?	**No** •
D.3.11.3.1	Somatic cell therapy medicinal product[16]?	**No** •
D.3.11.3.2	Gene therapy medicinal product[17]?	**No** •
D.3.11.3.3	Tissue Engineered Product[18]?	**No** •
D.3.11.3.4	Combination ATIMP (i.e. one involving a medical device[19])?	**No** •
D.3.11.3.5	Has the Committee on Advanced Therapies issued a classification for this product?	**No** •
D.3.11.3.5.1	If 'Yes' please provide that classification and its reference number:	
D.3.11.4	Combination product that includes a device, but does not involve an Advanced Therapy?	**No** •
D.3.11.5	Radiopharmaceutical medicinal product?	**No** •
D.3.11.6	Immunological medicinal product (such as vaccine, allergen, immune serum)?	**No** •
D.3.11.7	Plasma derived medicinal product?	**No** •
D.3.11.8	Extractive medicinal product?	**No** •
D.3.11.9	Recombinant medicinal product?	**No** •
D.3.11.10	Medicinal product containing genetically modified organisms?	**No** •
D.3.11.10.1	Has the authorisation for contained use or release been granted?	**No** •
D.3.11.10.2	Is it pending?	**No** •
D.3.11.11	Herbal medicinal product?	**No** •
D.3.11.12	Homeopathic medicinal product?	**No** •
D.3.11.13	Another type of medicinal product?	**No** •
D.3.11.13.1	If 'another type of medicinal product' specify the type of medicinal product:	
D.3.12	Mode of action (*free text* [20]) 5.1.1.c [redacted]	
D.3.13	Is it an IMP to be used in a first-in-human clinical trial?	**No** •
D.3.13.1	If 'Yes', are there risk factors identified, according to the guidance FIH?[21]	

D.4	**SOMATIC CELL THERAPY INVESTIGATIONAL MEDICINAL PRODUCT (NO GENETIC MODIFICATION)**	
D.4.1	Origin of cells	
D.4.1.1	Autologous	**No** •
D.4.1.2	Allogeneic	**No** •
D.4.1.3	Xenogeneic	**No** •
D.4.1.3.1	If 'Yes', specify the species of origin:	
D.4.2	Type of cells	
D.4.2.1	Stem cells	**No** •
D.4.2.2	Differentiated cells	**No** •
D.4.2.2.1	If 'Yes', specify the type (e.g. keratinocytes, fibroblasts, chondrocytes...):	
D.4.2.3	Others:	**No** •
D.4.2.3.1	If others, specify:	

D.5	**GENE THERAPY INVESTIGATIONAL MEDICINAL PRODUCTS**	
D.5.1	Gene(s) of interest:	
D.5.2	In vivo gene therapy:	**No** •
D.5.3	Ex vivo gene therapy:	**No** •
D.5.4	Type of gene transfer product	
D.5.4.1	Nucleic acid (e.g. plasmid): If 'Yes', specify if:	**No** •
D.5.4.1.1	Naked:	**No** •
D.5.4.1.2	Complexed	**No** •

D.5.4.2	Viral vector:	**No ●**
D.5.4.2.1	If 'Yes', specify the type: adenovirus, retrovirus, AAV, …:	
D.5.4.3	Others	**No ●**
D.5.4.3.1	If others, specify:	
D.5.5	Genetically modified somatic cells:	**No ●**
If 'Yes', specify the origin of the cells:		
D.5.5.1	Autologous:	**No ●**
D.5.5.2	Allogeneic:	**No ●**
D.5.5.3	Xenogeneic:	**No ●**
D.5.5.3.1	If 'Yes', specify the species of origin:	
D.5.5.4	Specify type of cells (hematopoietic stem cells…):	

D.6	**TISSUE ENGINEERED PRODUCT**	
The indication which determines that this is a Tissue Engineered Product as opposed to a Cell Therapy product is given in section E.1.1.		
D.6.1	Origin of cells	
D.6.1.1	Autologous	**No ●**
D.6.1.2	Allogeneic	**No ●**
D.6.1.3	Xenogeneic	**No ●**
D.6.1.3.1	If 'Yes', specify the species of origin:	
D.6.2	Type of cells	
D.6.2.1	Stem cells	**No ●**
D.6.2.2	Differentiated cells	**No ●**
D.6.2.2.1	If 'Yes', specify the type of cells(e.g. keratinocytes, fibroblasts, chondrocytes, …):	
D.6.2.3	Others:	**No ●**
D.6.2.3.1	If others, specify:	

D.7	**PRODUCTS CONTAINING DEVICES (i.e. MEDICAL DEVICES, SCAFFOLDS ETC.)**	
D.7.1	Give a brief description of the device:	
D.7.2	What is the name of the device?	
D.7.3	Is the device implantable?	**No ●**
D.7.4	Does this product contain:	
D.7.4.1	A medical device?	**No ●**
D.7.4.1.1	Does this medical device have a CE mark?	**No ●**
D.7.4.1.1.1	The notified body is:	
D.7.4.2	Bio-materials?	**No ●**
D.7.4.3	Scaffolds?	**No ●**
D.7.4.4	Matrices?	**No ●**
D.7.4.5	Other?	**No ●**
D.7.4.5.1	If other, specify:	

D.1	**IMP IDENTIFICATION**	
Indicate which of the following is described below, then repeat as necessary for each of the numbered IMPs to be used in the trial (assign numbers from 1-n):		
D.1.1	This refers to the IMP number:	**PR2**
D.1.2	IMP being tested	**Yes ●**
D.1.3	IMP used as a comparator	**No ●**

D.2	**STATUS OF THE IMP**

D.2.1	Has the IMP to be used in the trial a marketing authorisation?	**No ●**
If the IMP has a marketing authorisation in the Member State concerned by this application, but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2.		
D.2.1.1	If 'Yes', specify the product to be used in the clinical trial:	
D.2.1.1.1	Trade name	
D.2.1.1.1.1	EV Product Code (where applicable)	
D.2.1.1.2	Name of the Marketing Authorisation Holder:	
D.2.1.1.3	Marketing Authorisation number (if Marketing Authorisation granted by a Member State):	
D.2.1.1.4	Is the IMP modified in relation to its Marketing Authorisation?	**No ●**
D.2.1.1.4.1	If 'Yes', please specify:	
D.2.1.2	The country that granted the Marketing Authorisation	
D.2.1.2.1	Is this the Member State concerned with this application?	**No ●**

D.2.2	Situations where an IMP to be used in the CT has a Marketing Authorisation in the Member State concerned, but the protocol allows that any brand of the IMP with a Marketing Authorisation in that Member State be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start	
D.2.2.1	In the protocol, is treatment defined only by active substance?	**No ●**
D.2.2.1.1	If 'Yes', give active substance in D.3.8 or D.3.9	
D.2.2.2	In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?	**No ●**
D.2.2.2.1	If 'Yes', give active substance in D.3.8 or D.3.9	
D.2.2.3	The products to be administered as IMPs are defined as belonging to an ATC group[9]	**No ●**
D.2.2.3.1	If 'Yes', give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.3	
D.2.2.4	Other:	**No ●**
D.2.2.4.1	If 'Yes', please specify:	

D.2.3	IMPD submitted:	
D.2.3.1	Full IMPD:	**Yes ●**
D.2.3.2	Simplified IMPD:	**No ●**
D.2.3.3	Summary of product characteristics (SmPC) only:	**No ●**
D.2.4	Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?	**No ●**
D.2.4.1	If 'Yes' specify which Member States:	
D.2.5	Has the IMP been designated in this indication as an orphan drug in the Community?	**No ●**
D.2.5.1	If 'Yes', give the orphan drug designation number[10]:	

D.2.6	Has the IMP been the subject of scientific advice related to this clinical trial?	**No ●**
D.2.6.1	If 'Yes' to D.2.6, please indicate source of advice and provide a copy in the CTA request:	
D.2.6.1.1	CHMP[11]?	**No ●**
D.2.6.1.2	National Competent Authority?	**No ●**

D.3	**DESCRIPTION OF THE IMP**	
D.3.1	Product name where applicable[12]:	**Radioligand [11C]-UCB-J**
D.3.2	Product code where applicable[13]:	**[11C]-UCB-J**
D.3.3	ATC codes, if officially registered[14]:	

D.3.4	Pharmaceutical form (use standard terms):	**Solution for injection**
D.3.4.1	Is this a specific paediatric formulation?	**No ●**
D.3.5	Maximum duration of treatment of a subject according to the protocol: **1 minute**	
D.3.6	Dose allowed:	
D.3.6.1	For first trial only:	
	Specify per day or total	**Not Answered ●**
	Specify total dose (number and unit):	
	Route of administration (relevant to the first dose):	
D.3.6.2	For all trials	
	Specify per day or total	**Total ●**
	Specify total dose (number and unit):	**740 MBq megabecquerel(s)**
	Route of administration (relevant to the maximum dose):	**Intravenous bolus use (Noncurrent)**
D.3.7	Routes of administration (use standard terms):	**Intravenous bolus use (Noncurrent)**

D.3.8	Name of each active substance (INN or proposed INN if available):
D.3.9	Other available name for each active substance (provide all available):
D.3.9.1	CAS[15] number
D.3.9.2	Current sponsor code
D.3.9.3	Other descriptive name
D.3.9.4	EV Substance code
D.3.9.5	Full Molecular formula
D.3.9.6	Chemical/biological description of the Active Substance
D.3.10	Strength (specify all strengths to be used):
D.3.10.1	Concentration unit:
D.3.10.2	Concentration type ("exact number", "range", "more than" or "up to"):
D.3.10.3	Concentration (number).

D.3.11	Type of IMP	
Does the IMP contain an active substance:		
D.3.11.1	Of chemical origin?	**Yes ●**
D.3.11.2	Of biological / biotechnological origin (other than Advanced Therapy IMP (ATIMP)?	**No ●**
Is this a:		
D.3.11.3	Advanced Therapy IMP (ATIMP)?	**No ●**
D.3.11.3.1	Somatic cell therapy medicinal product[16]?	**No ●**
D.3.11.3.2	Gene therapy medicinal product[17]?	**No ●**
D.3.11.3.3	Tissue Engineered Product[18]?	**No ●**
D.3.11.3.4	Combination ATIMP (i.e. one involving a medical device[19])?	**No ●**
D.3.11.3.5	Has the Committee on Advanced Therapies issued a classification for this product?	**No ●**
D.3.11.3.5.1	If 'Yes' please provide that classification and its reference number:	
D.3.11.4	Combination product that includes a device, but does not involve an Advanced Therapy?	**No ●**
D.3.11.5	Radiopharmaceutical medicinal product?	**Yes ●**
D.3.11.6	Immunological medicinal product (such as vaccine, allergen, immune serum)?	**No ●**
D.3.11.7	Plasma derived medicinal product?	**No ●**
D.3.11.8	Extractive medicinal product?	**No ●**
D.3.11.9	Recombinant medicinal product?	**No ●**
D.3.11.10	Medicinal product containing genetically modified organisms?	**No ●**
D.3.11.10.1	Has the authorisation for contained use or release been granted?	**No ●**
D.3.11.10.2	Is it pending?	**No ●**

D.3.11.11	Herbal medicinal product?	**No ●**
D.3.11.12	Homeopathic medicinal product?	**No ●**
D.3.11.13	Another type of medicinal product?	**No ●**
D.3.11.13.1	If 'another type of medicinal product' specify the type of medicinal product:	
D.3.12	Mode of action (*free text* [20])	
D.3.13	Is it an IMP to be used in a first-in-human clinical trial?	**No ●**
D.3.13.1	If 'Yes', are there risk factors identified, according to the guidance FIH?[21]	

D.4	**SOMATIC CELL THERAPY INVESTIGATIONAL MEDICINAL PRODUCT (NO GENETIC MODIFICATION)**	
D.4.1	Origin of cells	
D.4.1.1	Autologous	**No ●**
D.4.1.2	Allogeneic	**No ●**
D.4.1.3	Xenogeneic	**No ●**
D.4.1.3.1	If 'Yes', specify the species of origin:	
D.4.2	Type of cells	
D.4.2.1	Stem cells	**No ●**
D.4.2.2	Differentiated cells	**No ●**
D.4.2.2.1	If 'Yes', specify the type (e.g. keratinocytes, fibroblasts, chondrocytes…):	
D.4.2.3	Others:	**No ●**
D.4.2.3.1	If others, specify:	

D.5	**GENE THERAPY INVESTIGATIONAL MEDICINAL PRODUCTS**	
D.5.1	Gene(s) of interest:	
D.5.2	In vivo gene therapy:	**No ●**
D.5.3	Ex vivo gene therapy:	**No ●**
D.5.4	Type of gene transfer product	
D.5.4.1	Nucleic acid (e.g. plasmid):	**No ●**
	If 'Yes', specify if:	
D.5.4.1.1	Naked:	**No ●**
D.5.4.1.2	Complexed	**No ●**
D.5.4.2	Viral vector:	**No ●**
D.5.4.2.1	If 'Yes', specify the type: adenovirus, retrovirus, AAV, …:	
D.5.4.3	Others	**No ●**
D.5.4.3.1	If others, specify:	
D.5.5	Genetically modified somatic cells:	**No ●**
If 'Yes', specify the origin of the cells:		
D.5.5.1	Autologous:	**No ●**
D.5.5.2	Allogeneic:	**No ●**
D.5.5.3	Xenogeneic:	**No ●**
D.5.5.3.1	If 'Yes', specify the species of origin:	
D.5.5.4	Specify type of cells (hematopoietic stem cells…):	

D.6	**TISSUE ENGINEERED PRODUCT**	
The indication which determines that this is a Tissue Engineered Product as opposed to a Cell Therapy product is given in section E.1.1.		
D.6.1	Origin of cells	
D.6.1.1	Autologous	**No ●**
D.6.1.2	Allogeneic	**No ●**
D.6.1.3	Xenogeneic	**No ●**
D.6.1.3.1	If 'Yes', specify the species of origin:	

D.6.2	Type of cells	
D.6.2.1	Stem cells	**No ●**
D.6.2.2	Differentiated cells	**No ●**
D.6.2.2.1	If 'Yes', specify the type of cells(e.g. keratinocytes, fibroblasts, chondrocytes, …):	
D.6.2.3	Others:	**No ●**
D.6.2.3.1	If others, specify:	

D.7	**PRODUCTS CONTAINING DEVICES (i.e. MEDICAL DEVICES, SCAFFOLDS ETC.)**	
D.7.1	Give a brief description of the device:	
D.7.2	What is the name of the device?	
D.7.3	Is the device implantable?	**No ●**
D.7.4	Does this product contain:	
D.7.4.1	A medical device?	**No ●**
D.7.4.1.1	Does this medical device have a CE mark?	**No ●**
D.7.4.1.1.1	The notified body is:	
D.7.4.2	Bio-materials?	**No ●**
D.7.4.3	Scaffolds?	**No ●**
D.7.4.4	Matrices?	**No ●**
D.7.4.5	Other?	**No ●**
D.7.4.5.1	If other, specify:	

D.8 INFORMATION ON PLACEBO (if relevant; repeat as necessary)

D.8.1	Is there a placebo:	**Yes ●**

D.8.2	This refers to placebo number:	**PL1**
D.8.3	Pharmaceutical form:	**Capsule**
D.8.4	Route of administration:	**Oral use**
D.8.5	Which IMP is it a placebo for? Specify IMP Number(s) from D.1.1	**PR1**
D.8.5.1	Composition, apart from the active substance(s):	
D.8.5.2	Is it otherwise identical to the IMP?	**Yes ●**
D.8.5.2.1	If not, specify major ingredients:	

D.9 SITE(S) WHERE THE QUALIFIED PERSON CERTIFIES BATCH RELEASE [22]

*This section is dedicated to **finished** IMPs, i.e. medicinal products randomised, packaged, labelled and certified for use in the clinical trial. If there is more than one site or more than one IMP is certified, use extra pages and give each IMP its number from section D.1.1 or D.8.2 In the case of multiple sites indicate the product certified by each site*

D.9.1	Do not fill in section D.9.2 for an IMP that: *Has a MA in the EU **and*** *Is sourced from the EU market **and*** *Is used in the trial without modification(e.g. not overencapsulated) **and*** *The packaging and labelling is carried out for local use only as per article 9.2. of the Directive 2005/28/EC (GCP Directive)* If all these conditions are met tick **?**and list the number(s) of each IMP including placebo from sections D.1.1 and D.8.2 to which this applies

D.9.2	**Who is responsible in the Community for the certification of the finished IMPs?**	
	This site is responsible for certification of (list the number(s) of each IMP including placebo from sections D.1.1 and D.8.2):	**PR1** **PL1**
	please tick the appropriate box:	
D.9.2.1	Manufacturer	**No •**
D.9.2.2	Importer	**Yes •**
D.9.2.3	Name of the organisation:	5.1.2.e [redacted]
D.9.2.4	Address:	
D.9.2.4.1	Street Address	5.1.2.e [redacted]
D.9.2.4.2	Town/City	5.1.2.e [redacted]
D.9.2.4.3	Post Code	5.1.2.e [redacted]
D.9.2.4.4	Country	5.1.2.e [redacted]
D.9.2.5	Give the manufacturing authorisation number:	5.1.2.e [redacted]
D.9.2.5.1	If No authorisation, give the reasons:	[redacted]

Where the product does not have a MA in the EU, but is supplied in bulk and final packaging and labelling for local use is carried out in accordance with article 9.2 of Directive 2005/28/EC (GCP Directive) then enter the site where the product was finally certified for release by the Qualified Person for use in the clinical trial at D.9.2 above.

D.9.2	**Who is responsible in the Community for the certification of the finished IMPs?**	
	This site is responsible for certification of (list the number(s) of each IMP including placebo from sections D.1.1 and D.8.2):	**PR2**
	please tick the appropriate box:	
D.9.2.1	Manufacturer	**Yes •**
D.9.2.2	Importer	**No •**
D.9.2.3	Name of the organisation:	**University Medical Center Groningen**
D.9.2.4	Address:	
D.9.2.4.1	Street Address	**Hanzeplein 1**
D.9.2.4.2	Town/City	**Groningen**
D.9.2.4.3	Post Code	**9713 AG**
D.9.2.4.4	Country	**Netherlands**
D.9.2.5	Give the manufacturing authorisation number:	**108964 F**
D.9.2.5.1	If No authorisation, give the reasons:	

Where the product does not have a MA in the EU, but is supplied in bulk and final packaging and labelling for local use is carried out in accordance with article 9.2 of Directive 2005/28/EC (GCP Directive) then enter the site where the product was finally certified for release by the Qualified Person for use in the clinical trial at D.9.2 above.

D.9.2	**Who is responsible in the Community for the certification of the finished IMPs?**	
	This site is responsible for certification of (list the number(s) of each IMP including placebo from sections D.1.1 and D.8.2):	**PR2**
	please tick the appropriate box:	
D.9.2.1	Manufacturer	**Yes •**
D.9.2.2	Importer	**No •**
D.9.2.3	Name of the organisation:	**Amsterdam UMC**
D.9.2.4	Address:	

D.9.2.4.1	Street Address	**De Boelelaan 1118**
D.9.2.4.2	Town/City	**Amsterdam**
D.9.2.4.3	Post Code	**1081 HZ**
D.9.2.4.4	Country	**Netherlands**
D.9.2.5	Give the manufacturing authorisation number:	**6682 F**
D.9.2.5.1	If No authorisation, give the reasons:	

Where the product does not have a MA in the EU, but is supplied in bulk and final packaging and labelling for local use is carried out in accordance with article 9.2 of Directive 2005/28/EC (GCP Directive) then enter the site where the product was finally certified for release by the Qualified Person for use in the clinical trial at D.9.2 above.

E. GENERAL INFORMATION ON THE TRIAL

This section should be used to provide information about the aims, scope and design of the trial. When the protocol includes a sub-study in the MS concerned section E.2.3 should be completed providing information about the sub-study. To identify it check the sub-study box in the 'Objective of the trial' question below.

E.1 MEDICAL CONDITION OR DISEASE UNDER INVESTIGATION

E.1.1 Specify the medical condition(s) to be investigated[23] (free text):
English **neurodegenerative diseases with synaptic dysfunction**

E.1.1.1 Medical condition in easily understood language
English **Alzheimer's disease**

E.1.1.2 Therapeutic area
Psychiatry and Psychology [F] - Mental Disorders [F03]

E.1.2 MedDRA version, system organ class, level, term and classification code[24]:

Version	System Organ Class	Classification Code	Term	Level
21.1	**10029205 - Nervous system disorders**	**10053643**	**Neurodegenerative disorder**	**PT**

E.1.3 Is any of the conditions being studied a rare disease[25]? **No ●**

E.2 OBJECTIVE OF THE TRIAL

E.2.1 Main objective:
English
Primary objective:
To assess the safety and tolerability of multiple, once-daily oral doses of RDN-929 over 28 days in healthy older adult subjects and early symptomatic Alzheimer's Disease (AD) subjects.

E.2.2 Secondary objectives:
English
Secondary:
To assess the plasma and CSF pharmacokinetics (PK) of RDN-929 in healthy older adult subjects and early symptomatic AD subjects.

Exploratory:
Part 1:
To explore the pharmacodynamics (PD) of RDN-929 in blood through analysis of peripheral blood mononuclear cells (PBMC) as well as synaptic and neuronal biomarkers in plasma and CSF in healthy older adult subjects.

Part 2:
To explore the pharmacodynamics (PD) of RDN-929 through analysis of synaptic and neuronal biomarkers in plasma and CSF in early symptomatic AD subjects.
To explore the change from baseline in quantitative Electroencephalography (qEEG) in early symptomatic AD subjects.
To assess the mean change from baseline in radioligand [11C]-UCB-J binding in pre-defined brain regions as measured by PET imaging in early symptomatic AD subjects.

Part 1 and 2:
To explore the change from baseline in clinical measures of cognition in healthy older adult subjects and early symptomatic AD subjects.

E.2.3 Is there a sub-study? **No ●**
E.2.3.1 If 'Yes', give the full title, date and version of each sub-study and their related objectives:

E.3	PRINCIPAL INCLUSION CRITERIA	*(list the most important)*
	English	**Adult males or postmenopausal or surgically sterile females age 55 – 85 years old for Part 1 and age 50 – 85 years old for Part 2, inclusive, at the time of informed consent.** **Body mass index (BMI) ≥18.0 kg/m2, <35.0 kg/m2 .** **Further inclusion criteria can be found in the protocol section 8.5.1.**

E.4	PRINCIPAL EXCLUSION CRITERIA	*(list the most important)*
	English	**History or current evidence of any clinically significant cardiovascular, endocrinologic, hematologic, hepatobiliary, immunologic, metabolic, urologic, pulmonary, neurologic (except for diagnosis of AD in Part 2), renal, or other major disease, as determined by the Investigator.** **Any conditions that, in the opinion of the Investigator, would make the subject unsuitable for enrollment or could interfere with the subject's participation in or completion of the study.** **Further exclusion criteria can be found in the protocol section 8.5.2**

E.5	END POINT(S):	
E.5.1	Primary End Point (repeat as necessary)[26]	
	English	**Safety parameters include adverse events (AEs), serious adverse events (SAEs), physical and neurological examination, clinical laboratory values, vital signs, 12-lead ECG, and C-SSRS scores.**
E.5.1.1	Timepoint(s) of evaluation of this end point	
	English	**Throughout the study**
E.5.2	Secondary End Point (repeat as necessary)	
	English	**Secondary Endpoints:** **Plasma PK and CSF parameters of RDN-929 such as Cmax and AUC as appropriate.** **Exploratory Endpoints:** **Part 1 and 2:** **PD parameters including selected biomarkers (within group changes and mean group differences).** **Part 1:** **PD parameters including PBMC post-translational modification (changes over time and mean group differences).** **Part 2:** **Quantitative Electroencephalography (qEEG), including resting state power spectral density (PSD), functional connectivity and Event Related Potential (ERP) acquired during neurocognitive tasks.** **Mean change in [11C]-UCB-J binding in pre-defined brain regions from baseline (Part 2 only) as measured by PET imaging.**
E.5.2.1	Timepoint(s) of evaluation of this end point	
	English	**Throughout the study**

E.6	SCOPE OF THE TRIAL – Tick all boxes where applicable		
E.6.1	Diagnosis		**No ●**
E.6.2	Prophylaxis		**No ●**
E.6.3	Therapy		**No ●**
E.6.4	Safety		**Yes ●**
E.6.5	Efficacy		**No ●**
E.6.6	Pharmacokinetic		**Yes ●**
E.6.7	Pharmacodynamic		**Yes ●**
E.6.8	Bioequivalence		**No ●**
E.6.9	Dose Response		**No ●**
E.6.10	Pharmacogenetic		**No ●**
E.6.11	Pharmacogenomic		**No ●**
E.6.12	Pharmacoeconomic		**No ●**
E.6.13	Others		**Yes ●**
E.6.13.1	If others, specify:		
	English	**qEEG, radioligand binding**	

E.7	TRIAL TYPE AND PHASE [27]		
E.7.1	Human pharmacology (Phase I)		**Yes ●**
Is it:			
E.7.1.1	First administration to humans		**No ●**
E.7.1.2	Bioequivalence study		**No ●**
E.7.1.3	Other:		**Yes ●**
E.7.1.3.1	If other, please specify:		
	English	**Pharmacokinetics**	
E.7.2	Therapeutic exploratory (Phase II)		**No ●**
E.7.3	Therapeutic confirmatory (Phase III)		**No ●**
E.7.4	Therapeutic use(Phase IV)		**No ●**

E.8	DESIGN OF THE TRIAL		
E.8.1	Controlled		**Yes ●**
	If 'Yes', specify:		
E.8.1.1	Randomised:		**Yes ●**
E.8.1.2	Open:		**No ●**
E.8.1.3	Single blind:		**No ●**
E.8.1.4	Double blind:		**Yes ●**
E.8.1.5	Parallel group:		**Yes ●**
E.8.1.6	Cross over:		**No ●**
E.8.1.7	Other:		**Yes ●**
E.8.1.7.1	If other specify:		
	English	**Part 2: open design**	
E.8.2	If controlled, specify the comparator:		
E.8.2.1	Other medicinal product(s)		**No ●**
E.8.2.2	Placebo		**Yes ●**
E.8.2.3	Other		**No ●**
E.8.2.3.1	If 'Yes' to other, specify :		
E.8.2.4	Number of treatment arms in the trial		**4**
E.8.3	Single site in the Member State concerned (see also section G):		**No ●**
E.8.4	Multiple sites in the Member State concerned(see also section G):		**Yes ●**
E.8.4.1	Number of sites anticipated in Member State concerned		**3**
E.8.5	Multiple Member States:		**No ●**
E.8.5.1	Number of sites anticipated in the EEA:		
E.8.6	Trial involving sites outside the EEA:		
E.8.6.1	Trial being conducted both within and outside the EEA:		**No ●**
E.8.6.2	Trial being conducted completely outside of the EEA:		**No ●**
E.8.6.3	If E.8.6.1 or E.8.6.2 are Yes, specify the regions in which trial sites are planned:		

E.8.6.4	If E.8.6.1 or E.8.6.2 are Yes, specify the number of sites anticipated outside of the EEA:	
E.8.7	Trial having an independent data monitoring committee:	**No ●**
E.8.8	Definition of the end of trial: If it is the last visit of the last subject, please enter "LVLS". If it is not LVLS provide the definition: **English** **LSLV**	
E.8.9	Initial estimate of the duration of the trial[28] (years, months and days)	
E.8.9.1	In the Member State concerned	**years 9 months days**
E.8.9.2	In all countries concerned by the trial	**years months days**
E.8.10	Proposed date of start of recruitment	
E.8.10.1	In the Member State concerned	**2019-05-15**
E.8.10.2	In any country	

F. POPULATION OF TRIAL SUBJECTS

F.1	**AGE RANGE**		
F.1.1	Are the trial subjects under 18? If 'Yes', specify the estimated number of subjects planned in each age range for the whole trial:		**No ●**
		Approx. No. of patients[29]	
F.1.1.1	In utero	()	**No ●**
F.1.1.2	Preterm newborn infants (up to gestational age < 37 weeks)	()	**No ●**
F.1.1.3	Newborns (0-27 days)	()	**No ●**
F.1.1.4	Infants and toddlers (28 days - 23 months)	()	**No ●**
F.1.1.5	Children (2-11 years)	()	**No ●**
F.1.1.6	Adolescents (12-17 years)	()	**No ●**
F.1.2	Adults (18-64 years)	(**15**)	**Yes ●**
F.1.3	Elderly (>= 65 years)	(**20**)	**Yes ●**

F.2	**GENDER**	
F.2.1	Female	**Yes ●**
F.2.2	Male	**Yes ●**

F.3	**GROUP OF TRIAL SUBJECTS**	
F.3.1	Healthy volunteers	**Yes ●**
F.3.2	Patients	**Yes ●**
F.3.3	Specific vulnerable populations	**No ●**
F.3.3.1	Women of child bearing potential not using contraception	**No ●**
F.3.3.2	Women of child bearing potential using contraception	**No ●**
F.3.3.3	Pregnant women	**No ●**
F.3.3.4	Nursing women	**No ●**
F.3.3.5	Emergency situation	**No ●**
F.3.3.6	Subjects incapable of giving consent personally	**No ●**
F.3.3.6.1	If 'Yes', specify:	
F.3.3.7	Others:	**No ●**
F.3.3.7.1	If 'Yes', specify:	

F.4	**PLANNED NUMBER OF SUBJECTS TO BE INCLUDED:**	
F.4.1	In the member state	**35**
F.4.2	For a multinational trial:	
F.4.2.1	In the EEA	**35**
F.4.2.2	In the whole clinical trial	**35**

F.5	**PLANS FOR TREATMENT OR CARE AFTER THE SUBJECT HAS ENDED HIS/HER PARTICIPATION IN THE TRIAL. please specify** (free text):
	English **None**

G. CLINICAL TRIAL SITES/INVESTIGATORS IN THE MEMBER STATE CONCERNED BY THIS REQUEST

G.1	**CO-ORDINATING INVESTIGATOR** (for multicentre trial) and principal investigator (for single centre trial)	
G.1.1	Given name:	[redacted]
G.1.2	Middle name, if applicable:	
G.1.3	Family name:	[redacted]
G.1.4	Qualification (MD..........)	[redacted]
G.1.5	Professional address:	
G.1.5	Institution name	**QPS Netherlands B.V.**
G.1.5	Institution department	**Clinical Pharmacology**
G.1.5.1	Street address	**Petrus Campersingel 123**
G.1.5.2	Town/city	**Groningen**
G.1.5.3	Post code	**9713 AG**
G.1.5.4	Country	**Netherlands**
G.1.6	Telephone number:	**+31 050 304**[redacted]
G.1.7	Fax number:	**+31 050 304**[redacted]
G.1.8	E-mail:	[redacted]**@qps.com**

G.1	**CO-ORDINATING INVESTIGATOR** (for multicentre trial) and principal investigator (for single centre trial)	
G.1.1	Given name:	[redacted]
G.1.2	Middle name, if applicable:	
G.1.3	Family name:	[redacted]
G.1.4	Qualification (MD..........)	[redacted]
G.1.5	Professional address:	
G.1.5	Institution name	**UMCG**
G.1.5	Institution department	**Alzheimer Center Groningen**
G.1.5.1	Street address	**Hanzeplein 1**
G.1.5.2	Town/city	**Groningen**
G.1.5.3	Post code	**9713 GZ**
G.1.5.4	Country	**Netherlands**
G.1.6	Telephone number:	
G.1.7	Fax number:	
G.1.8	E-mail:	

G.1	**CO-ORDINATING INVESTIGATOR** (for multicentre trial) and principal investigator (for single centre trial)	
G.1.1	Given name:	[redacted]
G.1.2	Middle name, if applicable:	
G.1.3	Family name:	[redacted]
G.1.4	Qualification (MD..........)	
G.1.5	Professional address:	
G.1.5	Institution name	**Amsterdam UMC**
G.1.5	Institution department	**Alzheimer Center Amsterdam**
G.1.5.1	Street address	**De Boelelaan 1118**
G.1.5.2	Town/city	**Amsterdam**
G.1.5.3	Post code	**1081 HZ**
G.1.5.4	Country	**Netherlands**
G.1.6	Telephone number:	
G.1.7	Fax number:	
G.1.8	E-mail:	

G.1	**CO-ORDINATING INVESTIGATOR** (for multicentre trial) and principal investigator (for single centre trial)	
G.1.1	Given name:	[redacted]

G.1.2	Middle name, if applicable:	
G.1.3	Family name:	[redacted]
G.1.4	Qualification (MD..........)	
G.1.5	Professional address:	
G.1.5	Institution name	**Brain Research Center BV**
G.1.5	Institution department	
G.1.5.1	Street address	**Cronenburg 2**
G.1.5.2	Town/city	**Amsterdam**
G.1.5.3	Post code	**1081 GN**
G.1.5.4	Country	**Netherlands**
G.1.6	Telephone number:	
G.1.7	Fax number:	
G.1.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***
G.2.1	Given name:
G.2.2	Middle name, if applicable:
G.2.3	Family name:
G.2.4	Qualification (MD..........)
G.2.5	Professional address:
G.2.5	Institution name
G.2.5	Institution department
G.2.5.1	Street address
G.2.5.2	Town/city
G.2.5.3	Post code
G.2.5.4	Country
G.2.6	Telephone number:
G.2.7	Fax number:
G.2.8	E-mail:

G.3	**CENTRAL TECHNICAL FACILITIES TO BE USED IN THE CONDUCT OF THE TRIAL** **Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised** (repeat as needed for multiple organisations).	
G.3.1	Name of organisation:	[redacted]
G.3.2	Department	[redacted]
G.3.3	Name of contact person:	
G.3.3.1	Given name	[redacted]
G.3.3.2	Middle name	
G.3.3.3	Family name	[redacted]
G.3.4	Address:	
G.3.4.1	Street address	[redacted]
G.3.4.2	Town/city	[redacted]
G.3.4.3	Post code	[redacted]
G.3.4.4	Country	[redacted]
G.3.5	Telephone number:	[redacted]
G.3.6	Fax number:	[redacted]
G.3.7	E-mail:	[redacted]
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No •**
G.3.8.2	Clinical chemistry	**Yes •**
G.3.8.3	Clinical haematology	**Yes •**
G.3.8.4	Clinical microbiology	**No •**
G.3.8.5	Histopathology	**No •**
G.3.8.6	Serology/ endocrinology	**Yes •**
G.3.8.7	Analytical chemistry	**Yes •**
G.3.8.8	ECG analysis/ review	**No •**
G.3.8.9	Medical image analysis/ review - X-ray, MRI,	**No •**

	ultrasound, etc.	
G.3.8.10	Primary/ surrogate endpoint test	**No •**
G.3.8.11	Other Duties subcontracted?	**No •**
G.3.8.11.1	If 'Yes', specify the other duties	

G.3	**CENTRAL TECHNICAL FACILITIES TO BE USED IN THE CONDUCT OF THE TRIAL** **Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised** (repeat as needed for multiple organisations).	
G.3.1	Name of organisation:	[redacted] **V.**
G.3.2	Department	[redacted]
G.3.3	Name of contact person:	
G.3.3.1	Given name	[redacted]
G.3.3.2	Middle name	
G.3.3.3	Family name	[redacted]
G.3.4	Address:	
G.3.4.1	Street address	[redacted]
G.3.4.2	Town/city	[redacted]
G.3.4.3	Post code	[redacted]
G.3.4.4	Country	[redacted]
G.3.5	Telephone number:	[redacted]
G.3.6	Fax number:	
G.3.7	E-mail:	
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No •**
G.3.8.2	Clinical chemistry	**No •**
G.3.8.3	Clinical haematology	**No •**
G.3.8.4	Clinical microbiology	**No •**
G.3.8.5	Histopathology	**No •**
G.3.8.6	Serology/ endocrinology	**No •**
G.3.8.7	Analytical chemistry	**No •**
G.3.8.8	ECG analysis/ review	**No •**
G.3.8.9	Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	**No •**
G.3.8.10	Primary/ surrogate endpoint test	**No •**
G.3.8.11	Other Duties subcontracted?	**Yes •**
G.3.8.11.1	If 'Yes', specify the other duties	**PK analysis**

G.3	**CENTRAL TECHNICAL FACILITIES TO BE USED IN THE CONDUCT OF THE TRIAL** **Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised** (repeat as needed for multiple organisations).	
G.3.1	Name of organisation:	**UMCG**
G.3.2	Department	**Nuclear Medicine and Molecular Imaging**
G.3.3	Name of contact person:	
G.3.3.1	Given name	
G.3.3.2	Middle name	
G.3.3.3	Family name	
G.3.4	Address:	
G.3.4.1	Street address	**Hanzeplein 1**
G.3.4.2	Town/city	**Groningen**
G.3.4.3	Post code	**9713 GZ**
G.3.4.4	Country	
G.3.5	Telephone number:	
G.3.6	Fax number:	
G.3.7	E-mail:	
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No •**
G.3.8.2	Clinical chemistry	**No •**

G.3.8.3	Clinical haematology	**No ●**
G.3.8.4	Clinical microbiology	**No ●**
G.3.8.5	Histopathology	**No ●**
G.3.8.6	Serology/ endocrinology	**No ●**
G.3.8.7	Analytical chemistry	**No ●**
G.3.8.8	ECG analysis/ review	**No ●**
G.3.8.9	Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	**Yes ●**
G.3.8.10	Primary/ surrogate endpoint test	**No ●**
G.3.8.11	Other Duties subcontracted?	**No ●**
G.3.8.11.1	If 'Yes', specify the other duties	

G.3	**CENTRAL TECHNICAL FACILITIES TO BE USED IN THE CONDUCT OF THE TRIAL** **Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised** (repeat as needed for multiple organisations).	
G.3.1	Name of organisation:	**Amsterdam UMC**
G.3.2	Department	**Radiology and Nuclear Medicine**
G.3.3	Name of contact person:	
G.3.3.1	Given name	
G.3.3.2	Middle name	
G.3.3.3	Family name	
G.3.4	Address:	
G.3.4.1	Street address	**De Boelelaan 1117**
G.3.4.2	Town/city	**Amsterdam**
G.3.4.3	Post code	**1081 HV**
G.3.4.4	Country	**Netherlands**
G.3.5	Telephone number:	
G.3.6	Fax number:	
G.3.7	E-mail:	
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No ●**
G.3.8.2	Clinical chemistry	**No ●**
G.3.8.3	Clinical haematology	**No ●**
G.3.8.4	Clinical microbiology	**No ●**
G.3.8.5	Histopathology	**No ●**
G.3.8.6	Serology/ endocrinology	**No ●**
G.3.8.7	Analytical chemistry	**No ●**
G.3.8.8	ECG analysis/ review	**No ●**
G.3.8.9	Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	**Yes ●**
G.3.8.10	Primary/ surrogate endpoint test	**No ●**
G.3.8.11	Other Duties subcontracted?	**No ●**
G.3.8.11.1	If 'Yes', specify the other duties	

G.3	**CENTRAL TECHNICAL FACILITIES TO BE USED IN THE CONDUCT OF THE TRIAL** **Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised** (repeat as needed for multiple organisations).	
G.3.1	Name of organisation:	**QPS Netherlands B.V.**
G.3.2	Department	**Clinical Pharmacology Unit Leeuwarden**
G.3.3	Name of contact person:	
G.3.3.1	Given name	
G.3.3.2	Middle name	
G.3.3.3	Family name	
G.3.4	Address:	
G.3.4.1	Street address	**Henri Dunantweg 6**
G.3.4.2	Town/city	**Leeuwarden**
G.3.4.3	Post code	**8934 AD**

G.3.4.4	Country	**Netherlands**
G.3.5	Telephone number:	
G.3.6	Fax number:	
G.3.7	E-mail:	
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No ●**
G.3.8.2	Clinical chemistry	**No ●**
G.3.8.3	Clinical haematology	**No ●**
G.3.8.4	Clinical microbiology	**No ●**
G.3.8.5	Histopathology	**No ●**
G.3.8.6	Serology/ endocrinology	**No ●**
G.3.8.7	Analytical chemistry	**No ●**
G.3.8.8	ECG analysis/ review	**Yes ●**
G.3.8.9	Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	**No ●**
G.3.8.10	Primary/ surrogate endpoint test	**No ●**
G.3.8.11	Other Duties subcontracted?	**No ●**
G.3.8.11.1	If 'Yes', specify the other duties	

G.3	**CENTRAL TECHNICAL FACILITIES TO BE USED IN THE CONDUCT OF THE TRIAL** **Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised** (repeat as needed for multiple organisations).	
G.3.1	Name of organisation:	**Brain Research Center BV**
G.3.2	Department	
G.3.3	Name of contact person:	
G.3.3.1	Given name	
G.3.3.2	Middle name	
G.3.3.3	Family name	
G.3.4	Address:	
G.3.4.1	Street address	**Cronenburg 2**
G.3.4.2	Town/city	**Amsterdam**
G.3.4.3	Post code	**1081 GN**
G.3.4.4	Country	**Netherlands**
G.3.5	Telephone number:	
G.3.6	Fax number:	
G.3.7	E-mail:	
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No ●**
G.3.8.2	Clinical chemistry	**No ●**
G.3.8.3	Clinical haematology	**No ●**
G.3.8.4	Clinical microbiology	**No ●**
G.3.8.5	Histopathology	**No ●**
G.3.8.6	Serology/ endocrinology	**No ●**
G.3.8.7	Analytical chemistry	**No ●**
G.3.8.8	ECG analysis/ review	**Yes ●**
G.3.8.9	Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	**No ●**
G.3.8.10	Primary/ surrogate endpoint test	**No ●**
G.3.8.11	Other Duties subcontracted?	**No ●**
G.3.8.11.1	If 'Yes', specify the other duties	

G.4	**NETWORKS TO BE INVOLVED IN THE TRIAL (e.g. Paediatric Networks involved in the trial)**
G.4.1	Name of organisation:
G.4.2	Name of contact person:
G.4.2.1	Given name
G.4.2.2	Middle name
G.4.2.3	Family name

G.4.3	Address:	
G.4.3.1	Street address	
G.4.3.2	Town/city	
G.4.3.3	Post code	
G.4.3.4	Country	
G.4.4	Telephone number:	
G.4.5	Fax number:	
G.4.6	E-mail:	
G.4.7	Activities carried out by the network:	

G.5	**ORGANISATIONS TO WHOM THE SPONSOR HAS TRANSFERRED TRIAL RELATED DUTIES AND FUNCTIONS**		
G.5.1	**Has the sponsor transferred any major or all the sponsor's trial related duties and functions to another organisation or third party?**		**Yes •**
Repeat as necessary for multiple organisations:			
G.5.1.1	Organisation name:	**QPS Netherlands B.V.**	
G.5.1.2	Organisation department		
G.5.1.3	Name of contact person :		
G.5.1.3.1	Given name	[redacted]	
G.5.1.3.2	Middle name		
G.5.1.3.3	Family name	[redacted]	
G.5.1.4	Address:		
G.5.1.4.1	Street address	**Petrus Campersingel 123**	
G.5.1.4.2	Town/city	**Groningen**	
G.5.1.4.3	Post code	**9713 AG**	
G.5.1.4.4	Country	**Netherlands**	
G.5.1.5	Telephone number:	**+31 50 304**[redacted]	
G.5.1.6	Fax number:		
G.5.1.7	E-mail:		
G.5.1.8	All tasks of the sponsor	**No •**	
G.5.1.9	Monitoring	**Yes •**	
G.5.1.10	Regulatory (e.g. preparation of applications to CA and ethics committee)	**Yes •**	
G.5.1.11	Investigator recruitment	**No •**	
G.5.1.12	IVRS[30] – treatment randomisation	**No •**	
G.5.1.13	Data management	**Yes •**	
G.5.1.14	E-data capture	**No •**	
G.5.1.15	SUSAR reporting	**No •**	
G.5.1.16	Quality assurance auditing	**No •**	
G.5.1.17	Statistical analysis	**Yes •**	
G.5.1.18	Medical writing	**Yes •**	
G.5.1.19	Other duties subcontracted?	**No •**	
G.5.1.19.1	If 'Yes' to other, please specify:		

G.5	**ORGANISATIONS TO WHOM THE SPONSOR HAS TRANSFERRED TRIAL RELATED DUTIES AND FUNCTIONS**		
G.5.1	**Has the sponsor transferred any major or all the sponsor's trial related duties and functions to another organisation or third party?**		**Yes •**
Repeat as necessary for multiple organisations:			
G.5.1.1	Organisation name:	[redacted]	
G.5.1.2	Organisation department		
G.5.1.3	Name of contact person :		
G.5.1.3.1	Given name		
G.5.1.3.2	Middle name		
G.5.1.3.3	Family name		
G.5.1.4	Address:		
G.5.1.4.1	Street address	[redacted].	
G.5.1.4.2	Town/city	[redacted]	

G.5.1.4.3	Post code	[redacted]
G.5.1.4.4	Country	[redacted]
G.5.1.5	Telephone number:	
G.5.1.6	Fax number:	
G.5.1.7	E-mail:	[redacted]
G.5.1.8	All tasks of the sponsor	**No** •
G.5.1.9	Monitoring	**No** •
G.5.1.10	Regulatory (e.g. preparation of applications to CA and ethics committee)	**No** •
G.5.1.11	Investigator recruitment	**No** •
G.5.1.12	IVRS[30] – treatment randomisation	**No** •
G.5.1.13	Data management	**No** •
G.5.1.14	E-data capture	**No** •
G.5.1.15	SUSAR reporting	**Yes** •
G.5.1.16	Quality assurance auditing	**No** •
G.5.1.17	Statistical analysis	**No** •
G.5.1.18	Medical writing	**No** •
G.5.1.19	Other duties subcontracted?	**No** •
G.5.1.19.1	If 'Yes' to other, please specify:	

H. COMPETENT AUTHORITY / ETHICS COMMITTEE IN THE MEMBER STATE CONCERNED BY THIS REQUEST

H.1	**TYPE OF APPLICATION**	
If this application is addressed to the Competent Authority, please tick the Ethics Committee box and give information on the Ethics committee concerned. If this application is addressed to the Ethics Committee, please tick the Competent Authority box and give the information on the Competent Authority concerned.		
H.1.1	Competent Authority	**No** ●
H.1.2	Ethics Committee	**Yes** ●

H.2	**INFORMATION ON ETHICS COMMITTEE**	
H.2.1	Name:	**Stichting Beoordeling Ethiek Biomedisch Onderzoek**
H.2.2	Address	
H.2.2.1	Street address	**Dr Nassaulaan 10**
H.2.2.2	Town/city	**Assen**
H.2.2.3	Post code	**9401 HK**
H.2.2.4	Country	**Netherlands**
H.2.3	Date of submission:	**2019-04-17**

H.3	**OPINION**	
H.3.1	To be requested	**Yes** ●
H.3.2	Pending	**No** ●
H.3.3	Given	**No** ●
	If 'Given', specify:	
H.3.3.1	Date of opinion:	
H.3.3.2	Opinion favourable	**No** ●
H.3.3.3	Opinion not favourable	**No** ●
	If not favourable, give:	
H.3.3.3.1	The reasons	
H.3.3.3.2	The eventual anticipated date of resubmission:	

I. SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

I.1	I hereby confirm that /confirm on behalf of the sponsor (delete which is not applicable) that: • the information provided is complete; • the attached documents contain an accurate account of the information available; • the clinical trial will be conducted in accordance with the protocol; and • the clinical trial will be conducted, and SUSARs and result-related information will be reported, in accordance with the applicable legislation.

I.2	**APPLICANT OF THE REQUEST FOR THE COMPETENT AUTHORITY** (as stated in section C.1):
I.2.1	Date: 14 October 2019
I.2.2	Signature[31]: [redacted] 5.1.2.e
I.2.3	Print name:

I.3	**APPLICANT OF THE REQUEST FOR THE ETHICS COMMITTEE** (as stated in section C.2):
I.3.1	Date:
I.3.2	Signature[32]:
I.3.3	Print name:

ENDNOTES

[1] Any translation of the protocol should be assigned the same date and version as those in the original document.
[2] International Standard Randomised Controlled Trial Number. Sponsors may wish to use an International Standardised Random Controlled Trial Number (ISRCTN) to identify their trial in addition to the EudraCT number; for instance if their trial is part of a multinational trial with sites outside the Community. They can obtain the number and guidance from the Current Controlled Trials website http://www.controlled-trials.com/isrctn to which there is a link from the EudraCT database website http://eudract.ema.europa.eu. When available they should provide it in Section A.6 of the application form.
[3] US National Clinical Trial (NCT) Numbers required on the FDA clinical trial application form.
[4] For a resubmission following previous withdrawal of an application or unfavourable opinion of an ethics committee, or previous withdrawal of an application or refusal of a request by the competent authority, enter a letter in the sequence, A for first resubmission, B for second, C for third et seq.
[5] In accordance with Article 19 of Directive 2001/20/EC.
[6] The contact point should give functional information rather than details of one "person", in order to avoid the need for update and maintenance of these contact details.
[7] This requires a EudraLink account. (See https://eudract.ema.europa.eu/document.html for details)
[8] According to national legislation.
[9] Available from the Summary of Product Characteristics (SmPC)
[10] According to the Community register on orphan medicinal products (Regulation (EC) n° 141/2000): http://ec.europa.eu/enterprise/pharmaceuticals/register/index.htm
[11] Committee for Medicinal Products for Human Use of the European Medicines Agency
[12] To be provided only when there is No trade name. This is the name routinely used by a sponsor to identify the IMP in the CT documentation (protocol, IB…).
[13] To be provided only when there is No trade name. This is a code designated by the sponsor which represents the name routinely used by the sponsor to identify the product in the CT documentation. For example, a code may be used for combinations of drugs or drugs and devices.
[14] Available from the Summary of Product Characteristics (SmPC).
[15] Chemical Abstracts Service.
[16] Complete also section D.4 Cell therapy as defined in Annex 1 part IV of Directive 2001/83/EC as amended.
[17] Complete also section D.5 Gene Therapy as defined in Annex 1 part IV of Directive 2001/83/EC as amended.
[18] Complete also section D.6 - Tissue Engineered Product as defined in Article 2(1)(b) of Regulation1394/2007/EC.
[19] Complete also section D.7
[20] The mode of action should briefly describe the chemical, biochemical, immunological or biological means the IMP uses to effect its pharmaceutical action.
[21] Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007 19 July 2007
[22] In accordance with paragraph 38 of Annex 13 of Volume 4 of the Rules Governing Medical Products in the European Union.
[23] In the case of healthy volunteer trials, the intended indication for the product under development should be provided.
[24] Applicants are encouraged to provide the MedDRA lower level term if applicable and classification code. These can be accessed from the EMEA EudraCT website (http://eudract.ema.europa.eu/).
[25] Points to consider on the calculation and reporting of the prevalence of a condition for Orphan drug designation: COM/436/01 (http://www.ema.europa.eu/htms/human/orphans/intro.htm).
[26] The protocol will usually identify a single primary end point but there may be a co-primary end point in some cases and/or a number of secondary end points.
[27] The descriptions of the trial types provided are those recommended in preference to Phases. See page 5 of Community guideline CPMP/ICH/291/95. The development of a new indication after initial approval of a medicine should be considered as a new development plan.
[28] From the first inclusion until the last visit of the last subject.
[29] These numbers will be initial estimates. Applicants will not be required to update this information nor do they constitute an authorisation or restriction on the inclusion of these numbers of patients in the trial. The numbers of subjects whose inclusion is authorised are those set out in the authorised version of the protocol, or subsequent authorised amendments.
[30] Interactive Voice Response System: commonly used for randomisation of treatment and controlling the shipment of stock of product.
[31] On an application to the Competent Authority only, the applicant to the Competent Authority needs to sign.

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

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 **:** ☐ Date :
Date of start of procedure:	Authorisation/ positive opinion **:** ☐ Date :
Competent authority registration number of the trial: Ethics committee registration number of the trial :	Withdrawal of amendment application ☐ 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.2 Notification for authorisation to the competent authority: ☒
A.3 Notification 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 parallel group study to assess the safety, tolerability and pharmacokinetic (PK) profile of multiple oral doses of RDN-929 in healthy older adults
B.4 Sponsor's protocol code number, version, and date: RDN-929-103, amendment 1, 19 June 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 : 300 Technology Square, 8th Floor, Life Sciences Suites, Cambridge, MA 02139, United States
C.1.4 Telephone number : n.a.p.
C.1.5 Fax number : n.ap.
C.1.6 e-mail: [redacted]@RodinTherapeutics.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:
C.2.2 Name of person to contact:
C.2.3 Address :
C.2.4 Telephone number :
C.2.5 Fax number :
C.2.6 e-mail:

D APPLICANT IDENTIFICATION (please tick the appropriate box)

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.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	
D.1.4.4	Telephone number : n.ap.	
D.1.4.5	Fax number : n.ap.	
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: ABR	
E.2.4	**Amendment to other documents or information:**	yes ☒ no ☐
E.2.4.1	If yes specify: ICF	
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)	
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 ( )	
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).* The consequences of the temporary halt for the evaluation of the results and for overall risk benefit assessment of the investigational medicinal product *(free text).*	

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 the track changes version of the protocol and the list of changes

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

G.1	Type of change
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

[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.1.3.3 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] ☐
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 [12]: [redacted] 5.1.2.e
J.2.2 Print name : [redacted] 5.1.2.e
J.2.3 Date : 14 October 2019

---

10 This requires a EudraLink account. (See https://eudract.ema.europa.eu/ for details)
11 Cf. Section 3.7.c. of the detailed guidance CT-1.

J.3	**APPLICANT OF THE REQUEST FOR THE ETHICS COMMITTEE (**as stated in section D.2):	☐
J.3.1	Signature [13]:	
J.3.2	Print name:	
J.3.3	Date :	

[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.

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

Groningen, 14 October 2019

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 I would like to ask the Competent Authority (Central Committee on Research Involving Human Subjects/Minister of Health, Welfare and Sport) to issue a certificate of no objection for a substantial amendment belonging to the research entitled *"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: With this amendment, the address of the sponsor was updated, the dosage level of Part 2 was set at 50 mg, the exclusion criterion regarding liver values at Screening was updated, the fasting requirement before clinical laboratory tests was updated, and a fasting requirement before PET scanning was added. Furthermore, sections describing stopping rules when liver values are increased 2x above ULN, describing additional one time hepatic assessments and describing study stopping rule were added.

Petrus Campersingel 123 • 9713 AG Groningen • P.O. BOX 137 • 9700 AC Groningen • The Netherlands
Email [redacted]@qps.com • Tel +31(0)50 304 [redacted] • Fax +31(0)50 304 [redacted]
Bank [redacted] IBAN [redacted] • BIC [redacted] • Trade Register 02083147 • VAT NL812888601B01

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 specified in question I1 of the general assessment and registration form (ABR form).

Kind regards

[redacted]

Petrus Campersingel 123 • 9713 AG Groningen • P.O. BOX 137 • 9700 AC Groningen • The Netherlands
Email [redacted]@qps.com • Tel +31(0)50 304 [redacted] • Fax +31(0)50 304 [redacted]
[redacted] • Trade Register 02083147 • VAT NL812888601B01

QPS helps you navigate

Enclosed documents

A1 - Cover letter applicant CCMO, 14 October 2019

B3 - EudraCT application form CCMO, 14 October 2019

B5 - EudraCT Substantial Amendment Form CCMO, 14 October 2019

QPS Netherlands BV
Petrus Campersingel 123 • 9713 AG Groningen • P.O. BOX 137 • 9700 AC Groningen • The Netherlands
Email [redacted] @qps.com • Tel +31(0)50 304 [redacted] Fax +31(0)50 304 [redacted]
[redacted] • Trade Register 02083147 • VAT NL812888601B01