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:	**2016-002976-28**
A.3	Full title of the trial:	
	English	**A randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's Disease (AD)**
A.3.1	Title of the trial for lay people, in easily understood, i.e. non-technical, language:	
	English	**To evaluate the efficacy and safety of CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's Disease (AD)**
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:	**CCNP520A2202J**
A.4.2	Sponsor's protocol version:	**v03**
A.4.3	Sponsor's protocol date:	**2020-01-07**
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:	**NCT03131453**
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:	**Novartis Pharma AG**
B.1.2	Name of the person to contact:	
B.1.2.1	Given name	5.1.2.e
B.1.2.2	Middle name	
B.1.2.3	Family name	5.1.2.e
B.1.3	Address:	
B.1.3.1	Street address	**Lichtstrasse 35**
B.1.3.2	Town/city	**Basel**
B.1.3.3	Post code	**CH-4056**
B.1.3.4	Country	**Switzerland**
B.1.4	Telephone number:	**+41** 5.1.2.e
B.1.5	Fax number:	
B.1.6	E-mail:	5.1.2.e **@novartis.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:	**Novartis Pharma Arzneimittel GmbH**
B.2.2	Name of person to contact:	
B.2.2.1	Given name	5.1.2.e
B.2.2.2	Middle name	
B.2.2.3	Family name	5.1.2.e
B.2.3	Address:	
B.2.3.1	Street address	**Roonstrasse 25**
B.2.3.2	Town/city	**Nürnberg**
B.2.3.3	Post code	**D-90429**
B.2.3.4	Country	**Germany**
B.2.4	Telephone number:	**+49** 5.1.2.e
B.2.5	Fax number:	**+49** 5.1.2.e
B.2.6	E-mail:	5.1.2.e **@novartis.com**

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:	**Novartis Pharma AG**
B.4.2	Country:	**Switzerland**

B.5	Contact point[6] designated by the sponsor for further information on the trial	
B.5.1	Name of organisation:	**Novartis Pharma AG**
B.5.2	Functional name of contact point (e.g. "Clinical Trial Information Desk"):	**Clinical Trial Information Desk**
B.5.3	Address:	
B.5.3.1	Street address	**Lichtstrasse 35**
B.5.3.2	Town/city	**Basel**
B.5.3.3	Post code	**CH-4056**
B.5.3.4	Country	**Switzerland**
B.5.4	Telephone number:	**+44** 5.1.2.e
B.5.5	Fax number:	**+44** 5.1.2.e
B.5.6	E-mail: (use a functional e-mail address rather than a personal one)	5.1.2.e **@novartis.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:	**Parexel International Romania s.r.l.**
C.1.4.2	Name of contact person:	
C.1.4.2.1	Given name	5.1.2.e
C.1.4.2.2	Middle name	
C.1.4.2.3	Family name	5.1.2.e
C.1.4.3	Address:	
C.1.4.3.1	Street address	**89-97 Grigore Alexandrescu St.**
C.1.4.3.2	Town/city	**Bucharest**
C.1.4.3.3	Post code	**010624**
C.1.4.3.4	Country	**Romania**
C.1.4.4	Telephone number:	**+40** 5.1.2.e
C.1.4.5	Fax number:	**+40** 5.1.2.e
C.1.4.6	E-mail:	5.1.2.e **@novartis.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?	**Not Answered •**
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?	**Not Answered •**
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?	**Not Answered •**
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]	**Not Answered •**
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:	**Not Answered •**
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	**Yes •**

	clinical trial conducted by the sponsor in the Community?	
D.2.4.1	If 'Yes' specify which Member States:	**Belgium** **Finland** **France** **Germany** **Iceland** **Italy** **Netherlands** **Portugal** **Spain** **United Kingdom**
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?	**Yes •**
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]?	**Yes •**
D.2.6.1.2	National Competent Authority?	**No •**

D.3	**DESCRIPTION OF THE IMP**	
D.3.1	Product name where applicable[12]:	**CNP520 15 mg**
D.3.2	Product code where applicable[13]:	**CNP520**
D.3.3	ATC codes, if officially registered[14]:	
D.3.4	Pharmaceutical form (use standard terms):	**Capsule, hard**
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:	
	96 months	
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	**Per day •**
	Specify total dose (number and unit):	**15 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):	
	Not established	
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	**CNP520**
D.3.9.3	Other descriptive name	
D.3.9.4	EV Substance code	**SUB166276**
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:	**mg milligram(s)**
D.3.10.2	Concentration type ("exact number", "range", "more than" or "up to"):	**equal**

D.3.10.3	Concentration (number).	**15**

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]) **CNP520 is an orally active beta-secretase (BACE-1) inhibitor**	
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.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?	**Not Answered •**
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?	**Not Answered •**
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?	**Not Answered •**
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]	**Not Answered •**
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:	**Not Answered •**
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?	**Yes •**
D.2.4.1	If 'Yes' specify which Member States:	**Belgium** **Finland** **France** **Germany** **Iceland** **Italy** **Netherlands** **Portugal**

		Spain **United Kingdom**
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?	**Yes •**
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]?	**Yes •**
D.2.6.1.2	National Competent Authority?	**No •**

D.3	**DESCRIPTION OF THE IMP**	
D.3.1	Product name where applicable[12]:	**CNP520 50 mg**
D.3.2	Product code where applicable[13]:	**CNP520**
D.3.3	ATC codes, if officially registered[14]:	
D.3.4	Pharmaceutical form (use standard terms):	**Capsule, hard**
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:	
	96 months	
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	**Per day •**
	Specify total dose (number and unit):	**50 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):	
	Not established	
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	**CNP520**
D.3.9.3	Other descriptive name	
D.3.9.4	EV Substance code	**SUB166276**
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:	**mg milligram(s)**
D.3.10.2	Concentration type ("exact number", "range", "more than" or "up to"):	**equal**
D.3.10.3	Concentration (number).	**50**

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]) **CNP520 is an orally active beta-secretase (BACE-1) inhibitor**	
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.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, hard**
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?	**No •**
D.8.5.2.1	If not, specify major ingredients:	
	5.1.1.c [redacted]	
D.8.5	Which IMP is it a placebo for? Specify IMP Number(s) from D.1.1	**PR2**
D.8.5.1	Composition, apart from the active substance(s):	
D.8.5.2	Is it otherwise identical to the IMP?	**No •**
D.8.5.2.1	If not, specify major ingredients:	
	5.1.1.c [redacted]	

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** **PR2** **PL1**
	please tick the appropriate box:	
D.9.2.1	Manufacturer	**Yes •**
D.9.2.2	Importer	**Yes •**
D.9.2.3	Name of the organisation:	**Novartis Pharma Arzneimittel GmbH**
D.9.2.4	Address:	
D.9.2.4.1	Street Address	**Roonstrasse 25**
D.9.2.4.2	Town/City	**Nürnberg**
D.9.2.4.3	Post Code	**D-90429**
D.9.2.4.4	Country	**Germany**
D.9.2.5	Give the manufacturing authorisation number:	5.1.1.c [redacted]
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** **Alzheimer's disease**
E.1.1.1	Medical condition in easily understood language **English** **Dementia**
E.1.1.2	Therapeutic area **Diseases [C] - Nervous System Diseases [C10]**
E.1.2	MedDRA version, system organ class, level, term and classification code[24]:

Version	System Organ Class	Classification Code	Term	Level
20.0	**100000004852**	**10001896**	**Alzheimer's disease**	**LLT**

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** **- To demonstrate the effect of CNP520 vs placebo on time to diagnosis of MCI due to AD or dementia due to AD, whichever occurs first during the course of the study.** **- To demonstrate the effect of CNP520 vs placebo on cognition using APCC.**
E.2.2	Secondary objectives: **English** **Key secondary objective:** **- To demonstrate the effects of CNP520 vs placebo on global clinical status.** **Secondary objectives:** **- To demonstrate the safety and tolerability of CNP520 vs placebo.** **- To demonstrate the effects of CNP520 vs placebo on cognition using Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).** **- To demonstrate the effects of CNP520 vs placebo on function.** **- To demonstrate the effects of CNP520 vs placebo on Magnetic Resonance Imaging (MRI) measures suggestive of cerebral amyloid angiopathy (CAA).** **- To demonstrate the effects of CNP520 vs placebo on brain atrophy.** **- To demonstrate the effects of CNP520 vs placebo on AD-related biomarkers.**
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 **Screening part I: Participants eligible for inclusion must fulfill all of the following criteria prior to scheduling the genetic disclosure.** **1. Written informed consent must be obtained before any assessment is performed as part of the study, including consent to receive disclosure of their risk estimates to develop clinical symptoms of AD based on their APOE genotype and, if HTs, with evidence of elevated brain amyloid.** **2. Male or female, age 60-75 years inclusive, at the time of signing the informed consent. To ensure that no more than 20% of participants in**

	the age group 60-64 years are randomized across the whole recruitment period, a site level process will be implemented. **3. Females must be considered post-menopausal and not of child bearing potential i.e. they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g. history of vasomotor symptoms), or have had surgical bilateral oophorectomy (with or without hysterectomy), total hysterectomy, or tubal ligation.** **4. Intellectually, visually and auditorily capable, fluent in, and able to read, the language in which study assessments are administered (e.g. completion of at least 6 years of regular schooling or sustained employment or equivalent local level of knowledge).** **5. Mini-Mental State Examination total score ≥24.** **6. Willing to have a study partner throughout the study.** **Screening part II: Participants eligible for inclusion must fulfill all of the following criteria prior to randomization based on the results from the screening test procedures.** **7. Carrier of at least one ε4 allele of the APOE gene: HMs with elevated or not elevated brain amyloid OR HTs with elevated brain amyloid (as measured in CSF collected via lumbar puncture or by amyloid PET imaging).** **Note: In cases where both lumbar puncture (CSF) amyloid and amyloid PET imaging tests are performed, at least one should be indicative of elevated brain amyloid.** **8. Cognitively unimpaired at screening visit as defined by: Score of 85 or greater on the RBANS delayed memory index score AND CDR global score of 0 with two special exceptions: a) If the RBANS delayed memory index score is between 70 and 84 (inclusive) AND the global CDR = 0, the participant may be allowed to continue ONLY if the investigator judges that cognition is unimpaired following review of the MCI/dementia criteria; b) If the global CDR score = 0.5 AND the RBANS delayed memory index score is 85 or greater, the participant may be allowed to continue ONLY if the investigator judges that cognition is unimpaired following review of the MCI/dementia criteria.** **9. Having a study partner who agrees to participate in the study and who is intellectually, visually, and auditorily capable, and fluent in, and able to read, the language in which study assessments are administered. Additionally, the study partner must be capable of and willing to: a) Accompany the participant to visits that requires the input of the study partner; b) Meet the definition of a "study partner".** **Other protocol defined inclusion criteria may apply.**

E.4	**PRINCIPAL EXCLUSION CRITERIA *(list the most important)***
English	**Screening part I: Participants will be excluded if they fulfill any of the following criteria prior to scheduling the genetic disclosure.** **1. Current medical or neurological condition that might impact cognition or performance on cognitive assessments e.g. MCI, dementia, Huntington's or Parkinson's disease etc.** **2. Advanced, severe progressive or unstable disease that may interfere with the safety, tolerability and study assessments, or put the participant at special risk e.g. active hepatitis, HIV infection, severe renal impairment, severe hepatic impairment etc.** **3. History of malignancy of any organ system, treated or untreated, within the past 60 months, regardless of whether there is evidence of local recurrence or metastases. However, localized nonmalignant tumors not requiring systemic chemo- or radio-therapy, localized basal or squamous cell carcinoma of the skin, in-situ cervical cancer are permitted.** **4. Current treatment with Cholinesterase Inhibitors and/or another AD treatment.**

5. Clinically relevant depigmenting or hypopigmenting conditions or active/history of chronic urticaria in the past year.
6. Score "yes" on item 4 or 5 of the Suicidal Ideation section of the eCSSRS patient-reported outcome, if this ideation occurred in the past 6 months, or "yes" on any item of the Suicidal Behavior section, except for the "Non-Suicidal Self- Injurious Behavior", if this behavior occurred in the past 2 years prior to screening.
7. Lacking psychological readiness to receive APOE genotype/amyloid status results, as assessed based on investigator's judgement supported by the pre-disclosure rating scales: Geriatric Depression Scale total score >6; Six Item Subset Inventory of the modified State Trait Anxiety Inventory total score >17.
8. Use of other investigational drugs prior to screening until: Small molecules: after 5 half-lives, or within 30 days until the expected pharmacodynamic effect has returned to baseline, whichever is longer; Biologicals: blood concentration has returned to baseline (or below serological responder threshold) for antibodies induced by active immunotherapy; or 5 half-lives for monoclonal antibodies or other biologicals.
9. Treatment
a) in the 4 weeks prior to randomization with any drug or treatment known for the potential to cause major organ system toxicity i.e. drugs that may require periodic safety monitoring of a specific organ or body fluid.
b) in the 4 weeks prior to randomization and/or current treatment with any CNS active drugs with the exceptions.
10. Current chronic treatment (>3 months) with: Strong CYP3A4 inducers or inhibitors; Drugs with a narrow therapeutic index known to be primarily metabolized by CYP2C or CYP3A isoenzymes and sensitive P-gp substrates.
11. Violations of concomitant medication restrictions.
12. Donation or loss of 400 mL or more of blood within 8 weeks prior to screening blood sampling and/or lumbar puncture if applicable.
13. Contraindication or intolerance to MRI investigations.
Screening part II: Participants fulfilling any of the following criteria based on results from the screening test procedures will be excluded.
14. A positive drug screen, if, in the investigator's opinion, this is due to drug abuse. Participants with a positive drug screen not believed to be related to drug abuse can be re-screened.
15. Previous participation in a CNP520 study with >3-month exposure to active treatment.
16. Significantly abnormal laboratory results at screening, meeting the exclusionary alert values specified in the Laboratory Manual. If, in the opinion of the investigator, an abnormal finding is the result of a temporary condition, the laboratory test can be repeated.
17. Current significant ECG findings from central reader that are assessed as clinically significant by the investigator. QTc interval >500 ms is exclusionary.
18. Brain MRI results from the central reading showing findings unrelated to AD that, in the opinion of the investigator might be a leading cause of future cognitive decline, might pose a risk to the participant, or might confound MRI assessment for safety monitoring (e.g. extensive white matter lesions, stroke, cerebrovascular disease as evidenced by multiple lacunar infarcts ≤20 mm or single infarct >20 mm, evidence of cerebral contusion etc.).
19. If PET scans are scheduled for this participant: Total dosimetry above the acceptable exposure in the country when combining the previous or planned Nuclear Medicine Radiology exposure and the scheduled study PET scan(s).
20. If CSF sampling is scheduled for this participant: Contraindication to lumbar puncture e.g. low platelet count, abnormal prothrombin time

international normalized ratio, history of back surgery (except microdiscectomy or laminectomy over one level), signs or symptoms of intracranial pressure etc.
Other protocol defined exclusion criteria may apply.

E.5	**END POINT(S):**	
E.5.1	Primary End Point (repeat as necessary)[26]	
	English	**- Time to the first event with event defined as the first confirmed diagnosis of MCI due to AD or dementia due to AD.** **- Change from baseline to month 60 in APCC score.**
E.5.1.1	Timepoint(s) of evaluation of this end point	
	English	**- Baseline to month 60.** **- Baseline to month 60.**
E.5.2	Secondary End Point (repeat as necessary)	
	English	**- Change from baseline to month 60 in Clinical Dementia Rating Scale - Sum of Boxes (CDRSOB) score.** **- Frequencies, changes from baseline, Kaplan-Meyer estimates when applicable of: Adverse events; Skin events based on a centralized dermatological monitoring; Safety findings from brain structural MRI central reader; Laboratory tests; Vital signs; ECG findings; Prospective suicidality assessment (ideation and behavior) from eC-SSRS.** **- Change from baseline to month 60 in total RBANS score and individual neurocognitive domain index scores.** **- Change from baseline to month 60 in total score of the Everyday Cognitive (ECog) scale: ECogsubject and ECog-informant.** **- Number, intensity and location of microhemorrhages and white matter hyperintensities using the Wahlund scale, both as assessed by central MRI reader.** **- Change from baseline to month 60 on volume of brain regions as measured by volumetric MRI.** **- Change from baseline to 24 and 60 months on: amyloid deposition as measured by standardized uptake ratio (SUVR) of radiotracer positron emission tomography (PET) scan; CSF levels of Aβ40, Aβ42; neurodegeneration as measured by CSF levels of total tau and phosphorylated tau. Collected only in participants who consented to additional voluntary procedures.**
E.5.2.1	Timepoint(s) of evaluation of this end point	
	English	**- Baseline to month 60.** **- Baseline to month 60.** **- Baseline to month 60.** **- Baseline to month 60.** **- Baseline to month 60.** **- Baseline to month 60.** **- Baseline to month 24 and 60.**

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	**Yes •**
E.6.6	Pharmacokinetic	**Yes •**
E.6.7	Pharmacodynamic	**Yes •**
E.6.8	Bioequivalence	**No •**
E.6.9	Dose Response	**Yes •**

E.6.10	Pharmacogenetic	**Yes •**
E.6.11	Pharmacogenomic	**Yes •**
E.6.12	Pharmacoeconomic	**No •**
E.6.13	Others	**No •**
E.6.13.1	If others, specify:	

E.7	**TRIAL TYPE AND PHASE[27]**	
E.7.1	Human pharmacology (Phase I)	**No •**
Is it:		
E.7.1.1	First administration to humans	**No •**
E.7.1.2	Bioequivalence study	**No •**
E.7.1.3	Other:	**No •**
E.7.1.3.1	If other, please specify:	
E.7.2	Therapeutic exploratory (Phase II)	**Yes •**
E.7.3	Therapeutic confirmatory (Phase III)	**Yes •**
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:	**No •**
E.8.1.7.1	If other specify:	
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	**3**

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	**2**	
E.8.5	Multiple Member States:	**Yes •**	
E.8.5.1	Number of sites anticipated in the EEA:	**50**	
E.8.6	Trial involving sites outside the EEA:		
E.8.6.1	Trial being conducted both within and outside the EEA:	**Yes •**	
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:		

Argentina
Australia
Belgium
Canada
Chile
China
Finland
France
Germany
Iceland
Israel
Italy
Japan
Korea, Republic of
Mexico
Netherlands

	Portugal **Singapore** **South Africa** **Spain** **Switzerland** **Taiwan** **United Kingdom** **United States**	
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:	**129**
E.8.7	Trial having an independent data monitoring committee:	**Yes •**
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** **LVLS**	
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	**6 years 11 months days**
E.8.9.2	In all countries concerned by the trial	**7 years 6 months days**
E.8.10	Proposed date of start of recruitment	
E.8.10.1	In the Member State concerned	**2017-12-11**
E.8.10.2	In any country	**2017-08-03**

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:	Approx. No. of patients[29]	**No •**
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)	(**400**)	**Yes •**
F.1.3	Elderly (>= 65 years)	(**1600**)	**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	**No •**
F.3.2	Patients	**Yes •**
F.3.3	Specific vulnerable populations	**Yes •**
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:	**Yes •**
F.3.3.7.1	If 'Yes', specify:	
	English	**Participants at risk for the onset of clinical symptoms of AD**

F.4	PLANNED NUMBER OF SUBJECTS TO BE INCLUDED:	
F.4.1	In the member state	**30**
F.4.2	For a multinational trial**:**	
F.4.2.1	In the EEA	**708**
F.4.2.2	In the whole clinical trial	**2000**

F.5	PLANS FOR TREATMENT OR CARE AFTER THE SUBJECT HAS ENDED HIS/HER PARTICIPATION IN THE TRIAL. **please specify** (free text):	
	English	**Upon study completion (assuming futility was not met), participants may have the opportunity to enter an extension under a separate study, if eligible.**

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:
G.1.2	Middle name, if applicable:
G.1.3	Family name:
G.1.4	Qualification (MD…….)
G.1.5	Professional address:
G.1.5	Institution name
G.1.5	Institution department
G.1.5.1	Street address
G.1.5.2	Town/city
G.1.5.3	Post code
G.1.5.4	Country
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:	5.1.2.e
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	5.1.2.e
G.2.4	Qualification (MD…….)	5.1.2.e
G.2.5	Professional address:	
G.2.5	Institution name	**Brain Research Center Amsterdam**
G.2.5	Institution department	
G.2.5.1	Street address	**Cronenburg 2**
G.2.5.2	Town/city	**Amsterdam**
G.2.5.3	Post code	**1081GN**
G.2.5.4	Country	**Netherlands**
G.2.6	Telephone number:	**na**
G.2.7	Fax number:	**na**
G.2.8	E-mail:	

G.2	PRINCIPAL INVESTIGATORS *(for multicentre trial ; where necessary, use additional forms)*	
G.2.1	Given name:	5.1.2.e
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	5.1.2.e
G.2.4	Qualification (MD…….)	5.1.2.e
G.2.5	Professional address:	
G.2.5	Institution name	**Brain Research Center Den Bosch**
G.2.5	Institution department	
G.2.5.1	Street address	**Statenlaan 37**
G.2.5.2	Town/city	**'s Hertogenbosch**
G.2.5.3	Post code	**5223 LA**
G.2.5.4	Country	**Netherlands**
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:	5.1.1.c
G.3.2	Department	5.1.2.e
G.3.3	Name of contact person:	
G.3.3.1	Given name	5.1.2.e
G.3.3.2	Middle name	
G.3.3.3	Family name	5.1.2.e
G.3.4	Address:	
G.3.4.1	Street address	5.1.1.c
G.3.4.2	Town/city	5.1.1.c
G.3.4.3	Post code	5.1.1.c
G.3.4.4	Country	5.1.1.c
G.3.5	Telephone number:	5.1.2.e
G.3.6	Fax number:	5.1.2.e
G.3.7	E-mail:	5.1.2.e
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	**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	**Receipt of batch samples from centres/shipment to reference labs; sample analysis; lab supplies**

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:	5.1.1.c
G.3.2	Department	
G.3.3	Name of contact person:	
G.3.3.1	Given name	5.1.2.e
G.3.3.2	Middle name	
G.3.3.3	Family name	5.1.2.e
G.3.4	Address:	
G.3.4.1	Street address	5.1.1.c
G.3.4.2	Town/city	5.1.1.c
G.3.4.3	Post code	5.1.1.c
G.3.4.4	Country	5.1.1.c
G.3.5	Telephone number:	5.1.2.e
G.3.6	Fax number:	5.1.2.e
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	**Yes •**
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	**Yes •**
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	**Assay validation/transfer; sample 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:	5.1.1.c
G.3.2	Department	5.1.1.c
G.3.3	Name of contact person:	
G.3.3.1	Given name	5.1.2.e
G.3.3.2	Middle name	
G.3.3.3	Family name	5.1.2.e
G.3.4	Address:	
G.3.4.1	Street address	5.1.1.c
G.3.4.2	Town/city	5.1.1.c
G.3.4.3	Post code	5.1.1.c
G.3.4.4	Country	5.1.1.c
G.3.5	Telephone number:	5.1.2.e
G.3.6	Fax number:	
G.3.7	E-mail:	5.1.2.e
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?	**Yes •**
G.3.8.11.1	If 'Yes', specify the other duties	**Central reading re: ECG; eCSSRS**

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:	5.1.1.c
G.3.2	Department	5.1.1.c
G.3.3	Name of contact person:	
G.3.3.1	Given name	5.1.2.e
G.3.3.2	Middle name	
G.3.3.3	Family name	5.1.2.e
G.3.4	Address:	
G.3.4.1	Street address	5.1.1.c
G.3.4.2	Town/city	5.1.1.c
G.3.4.3	Post code	5.1.1.c
G.3.4.4	Country	5.1.1.c
G.3.5	Telephone number:	5.1.2.e
G.3.6	Fax number:	

G.3.7	E-mail:	5.1.2.e
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?	**Yes •**
G.3.8.11.1	If 'Yes', specify the other duties	**Site training; CRF/data review; central reading/image analysis/archiving of MRI and Tau PET scans**

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:	5.1.1.c
G.3.2	Department	
G.3.3	Name of contact person:	
G.3.3.1	Given name	5.1.2.e
G.3.3.2	Middle name	
G.3.3.3	Family name	5.1.2.e
G.3.4	Address:	
G.3.4.1	Street address	5.1.1.c
G.3.4.2	Town/city	5.1.1.c
G.3.4.3	Post code	5.1.1.c
G.3.4.4	Country	5.1.1.c
G.3.5	Telephone number:	5.1.2.e
G.3.6	Fax number:	
G.3.7	E-mail:	5.1.2.e
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?	**Yes •**
G.3.8.11.1	If 'Yes', specify the other duties	**Central dermatology, photography, monitoring & review; training**

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:	5.1.1.c
G.3.2	Department	5.1.2.e
G.3.3	Name of contact person:	

G.3.3.1	Given name	5.1.2.e
G.3.3.2	Middle name	
G.3.3.3	Family name	5.1.2.e
G.3.4	Address:	
G.3.4.1	Street address	5.1.1.c
G.3.4.2	Town/city	5.1.1.c
G.3.4.3	Post code	5.1.1.c
G.3.4.4	Country	5.1.1.c
G.3.5	Telephone number:	5.1.2.e
G.3.6	Fax number:	
G.3.7	E-mail:	5.1.2.e
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	**Supply of Amyloid PET ligand (flutemetamol) to various sites in various countries**

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:	5.1.1.c
G.3.2	Department	5.1.1.c
G.3.3	Name of contact person:	
G.3.3.1	Given name	5.1.2.e
G.3.3.2	Middle name	
G.3.3.3	Family name	5.1.2.e
G.3.4	Address:	
G.3.4.1	Street address	5.1.1.c
G.3.4.2	Town/city	5.1.1.c
G.3.4.3	Post code	5.1.1.c
G.3.4.4	Country	5.1.1.c
G.3.5	Telephone number:	5.1.2.e
G.3.6	Fax number:	
G.3.7	E-mail:	5.1.2.e
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?	**Yes •**
G.3.8.11.1	If 'Yes', specify the other duties	**Amyloid/Tau biomarker supply/expertise; PET reading/analysis/archiving; CRF/data review;**

	training

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:	5.1.1.c
G.3.2	Department	5.1.1.c
G.3.3	Name of contact person:	
G.3.3.1	Given name	5.1.2.e
G.3.3.2	Middle name	
G.3.3.3	Family name	5.1.2.e
G.3.4	Address:	
G.3.4.1	Street address	5.1.1.c
G.3.4.2	Town/city	5.1.1.c
G.3.4.3	Post code	5.1.1.c
G.3.4.4	Country	5.1.1.c
G.3.5	Telephone number:	5.1.2.e
G.3.6	Fax number:	
G.3.7	E-mail:	5.1.2.e
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	**Training; reading/archiving re:scales/MCI&AD diagnosis; adjudication;eSource data collection**

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**	**Yes •**

	party?	

Repeat as necessary for multiple organisations:

G.5.1.1	Organisation name:	**Parexel International GmbH**
G.5.1.2	Organisation department	**CTRS-PL**
G.5.1.3	Name of contact person :	
G.5.1.3.1	Given name	5.1.2.e
G.5.1.3.2	Middle name	
G.5.1.3.3	Family name	5.1.2.e
G.5.1.4	Address:	
G.5.1.4.1	Street address	**Klinikum Westend, Haus 18, Spandauer Damm 130**
G.5.1.4.2	Town/city	**Berlin**
G.5.1.4.3	Post code	**D-14050**
G.5.1.4.4	Country	**Germany**
G.5.1.5	Telephone number:	**+49** 5.1.2.e
G.5.1.6	Fax number:	**+49-** 5.1.2.e
G.5.1.7	E-mail:	5.1.2.e **@parexel.com**
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)	**Yes •**
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	**No •**
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:	

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:	5.1.1.c
G.5.1.2	Organisation department	5.1.1.c
G.5.1.3	Name of contact person :	
G.5.1.3.1	Given name	5.1.2.e
G.5.1.3.2	Middle name	
G.5.1.3.3	Family name	5.1.2.e
G.5.1.4	Address:	
G.5.1.4.1	Street address	5.1.1.c
G.5.1.4.2	Town/city	5.1.1.c
G.5.1.4.3	Post code	5.1.1.c
G.5.1.4.4	Country	5.1.1.c
G.5.1.5	Telephone number:	5.1.2.e
G.5.1.6	Fax number:	
G.5.1.7	E-mail:	5.1.2.e
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	**No •**

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?	**Yes •**
G.5.1.19.1	If 'Yes' to other, please specify:	**Regional warehousing/auxiliary labelling**

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:	5.1.1.c
G.5.1.2	Organisation department	5.1.1.c
G.5.1.3	Name of contact person :	
G.5.1.3.1	Given name	5.1.2.e
G.5.1.3.2	Middle name	
G.5.1.3.3	Family name	5.1.2.e
G.5.1.4	Address:	
G.5.1.4.1	Street address	5.1.1.c
G.5.1.4.2	Town/city	5.1.1.c
G.5.1.4.3	Post code	5.1.1.c
G.5.1.4.4	Country	5.1.1.c
G.5.1.5	Telephone number:	5.1.2.e
G.5.1.6	Fax number:	
G.5.1.7	E-mail:	5.1.2.e
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	**No •**
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?	**Yes •**
G.5.1.19.1	If 'Yes' to other, please specify:	**Regional warehousing/auxiliary labelling**

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:	5.1.1.c
G.5.1.2	Organisation department	5.1.1.c
G.5.1.3	Name of contact person :	
G.5.1.3.1	Given name	5.1.2.e
G.5.1.3.2	Middle name	
G.5.1.3.3	Family name	5.1.2.e
G.5.1.4	Address:	
G.5.1.4.1	Street address	5.1.1.c
G.5.1.4.2	Town/city	5.1.1.c
G.5.1.4.3	Post code	5.1.1.c
G.5.1.4.4	Country	5.1.1.c
G.5.1.5	Telephone number:	5.1.2.e
G.5.1.6	Fax number:	
G.5.1.7	E-mail:	5.1.2.e

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	**No •**
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?	**Yes •**
G.5.1.19.1	If 'Yes' to other, please specify:	**Regional warehousing/auiliary labelling**

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:	5.1.1.c
G.5.1.2	Organisation department	5.1.1.c
G.5.1.3	Name of contact person :	
G.5.1.3.1	Given name	5.1.2.e
G.5.1.3.2	Middle name	
G.5.1.3.3	Family name	5.1.2.e
G.5.1.4	Address:	
G.5.1.4.1	Street address	5.1.1.c
G.5.1.4.2	Town/city	5.1.1.c
G.5.1.4.3	Post code	5.1.1.c
G.5.1.4.4	Country	5.1.1.c
G.5.1.5	Telephone number:	5.1.2.e
G.5.1.6	Fax number:	
G.5.1.7	E-mail:	5.1.2.e
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	**Yes •**
G.5.1.13	Data management	**No •**
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	**No •**
G.5.1.18	Medical writing	**No •**
G.5.1.19	Other duties subcontracted?	**Yes •**
G.5.1.19.1	If 'Yes' to other, please specify:	**Subject randomization management; Drug supply management; IRT services**

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:	5.1.1.c
G.5.1.2	Organisation department	
G.5.1.3	Name of contact person :	
G.5.1.3.1	Given name	5.1.2.e

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	5.1.1.c
G.5.1.4.2	Town/city	5.1.1.c
G.5.1.4.3	Post code	5.1.1.c
G.5.1.4.4	Country	5.1.1.c
G.5.1.5	Telephone number:	
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	**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	**No •**
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?	**Yes •**
G.5.1.19.1	If 'Yes' to other, please specify:	**Long term Sample storage and shipments**

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:	5.1.1.c
G.5.1.2	Organisation department	5.1.2.e
G.5.1.3	Name of contact person :	
G.5.1.3.1	Given name	5.1.2.e
G.5.1.3.2	Middle name	
G.5.1.3.3	Family name	5.1.2.e
G.5.1.4	Address:	
G.5.1.4.1	Street address	5.1.1.c
G.5.1.4.2	Town/city	5.1.1.c
G.5.1.4.3	Post code	5.1.1.c
G.5.1.4.4	Country	5.1.1.c
G.5.1.5	Telephone number:	5.1.2.e
G.5.1.6	Fax number:	5.1.2.e
G.5.1.7	E-mail:	5.1.2.e
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	**No •**
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?	**Yes •**
G.5.1.19.1	If 'Yes' to other, please specify:	**Protocol, analysis plan & IDMC review; SAE programming & SAE narratives; IDMC reports & liaison**

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:	5.1.1.c
G.5.1.2	Organisation department	
G.5.1.3	Name of contact person :	
G.5.1.3.1	Given name	5.1.2.e
G.5.1.3.2	Middle name	
G.5.1.3.3	Family name	5.1.2.e
G.5.1.4	Address:	
G.5.1.4.1	Street address	5.1.1.c
G.5.1.4.2	Town/city	5.1.1.c
G.5.1.4.3	Post code	5.1.1.c
G.5.1.4.4	Country	5.1.1.c
G.5.1.5	Telephone number:	5.1.2.e
G.5.1.6	Fax number:	
G.5.1.7	E-mail:	5.1.2.e
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	**No •**
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?	**Yes •**
G.5.1.19.1	If 'Yes' to other, please specify:	5.1.1.c **Data collection and management**

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:	5.1.1.c
G.5.1.2	Organisation department	
G.5.1.3	Name of contact person :	
G.5.1.3.1	Given name	5.1.2.e
G.5.1.3.2	Middle name	
G.5.1.3.3	Family name	5.1.2.e
G.5.1.4	Address:	
G.5.1.4.1	Street address	5.1.1.c
G.5.1.4.2	Town/city	5.1.1.c
G.5.1.4.3	Post code	5.1.1.c
G.5.1.4.4	Country	5.1.1.c
G.5.1.5	Telephone number:	5.1.2.e
G.5.1.6	Fax number:	
G.5.1.7	E-mail:	5.1.2.e
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	**No •**
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?	**Yes •**
G.5.1.19.1	If 'Yes' to other, please specify:	**Implementation and management of study website; Management of site recruitment tools; Travel support**

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:	5.1.1.c
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	5.1.1.c
G.5.1.4.2	Town/city	5.1.1.c
G.5.1.4.3	Post code	5.1.1.c
G.5.1.4.4	Country	5.1.1.c
G.5.1.5	Telephone number:	
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	**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	**No •**
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?	**Yes •**
G.5.1.19.1	If 'Yes' to other, please specify:	**Rental of -70 freezer to BRC Den Bosch**

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:	**METc VUmc**
H.2.2	Address	
H.2.2.1	Street address	**van der Boechorststraat 7**
H.2.2.2	Town/city	**Amsterdam**
H.2.2.3	Post code	**1081 BT**
H.2.2.4	Country	**Netherlands**
H.2.3	Date of submission:	**2017-09-19**

H.3	**OPINION**	
H.3.1	To be requested	**No ●**
H.3.2	Pending	**No ●**
H.3.3	Given	**Yes ●**
	If 'Given', specify:	
H.3.3.1	Date of opinion:	**2018-07-06**
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:
I.2.2	Signature[31]:
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.