Declaration of the End of Trial Form (cf. Section 4.2.1 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 THE END OF A CLINICAL TRIAL OF A MEDICINE FOR HUMAN USE TO THE COMPETENT AUTHORITY AND THE ETHICS COMMITTEE

For official use

Date of receipt :	Competent authority registration number : Ethics committee registration number:

To be filled in by the applicant

A MEMBER STATE IN WHICH THE DECLARATION IS BEING MADE : Netherlands

B TRIAL IDENTIFICATION

B.1 EudraCT number :	2016-002976-28
B.2 Sponsor's protocol code number:	CCNP520A2202J
B.3 Full title of the trial :	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)

C APPLICANT IDENTIFICATION (please tick the appropriate box)

C.1	**DECLARATION 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.	☒
C.1.4	**Complete below**:	
C.1.4.1	Organisation : Parexel International Romania s.r.l.	
C.1.4.2	Name of person to contact : 5.1.2.e	
C.1.4.3	Address : Metropolis Center, Str. Grigore Alexandrescu, No. 89-97, Bucharest, 010624, 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.2	**DECLARATION FOR THE ETHICS COMMITTEE**	☐
C.2.1	Sponsor	☐
C.2.2	Legal representative of the sponsor	☐
C.2.3	Person or organisation authorised by the sponsor to make the application.	☐
C.2.4	Investigator in charge of the application if applicable[2]:	
	• Co-ordinating investigator (for multicentre trial):	☐
	• Principal investigator (for single centre trial):	☐
C.2.5	**Complete below** :	
C.2.5.1	Organisation:	
C.2.5.2	Name :	
C.2.5.3	Address :	
C.2.5.4	Telephone number :	
C.2.5.5	Fax number :	
C.2.5.6	E-mail :	

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

2 According to national legislation.

D END OF TRIAL

D.1 Date of the end of the trial in this Member State ? [3]	yes ☒ no ☐
D.1.1. (YYYY/MM/DD): 2020/03/10	

D.2 Date of the end of the complete trial in all countries concerned by the trial? [3]	yes ☒ no ☐
D.2.1 (YYYY/MM/DD): 2020/03/26	

D.3 Is it an early termination? [4]	yes ☒ no ☐
D.3.1 If yes, give date (YYYY/MM/DD): 2019/07/08	

D.3.2 Briefly describe in an annex (free text):

D.3.2.1 The justification for early termination of the trial;

The Sponsor's decision to terminate early study CCNP520A2202J was made on July 8, 2019 and follows the assessment of unblinded data of the BACE1 inhibitor, CNP520, by the independent Data Monitoring Committee (DMC), during a planned data review on June 26, 2019.

Key findings from this data review of CNP520 were as follows:

- Consistent mild worsening was observed in some measures of cognitive function. Worse performance on RBANS was observed for CNP520 15 mg and CNP520 50 mg compared to placebo at both Week 13 and 26 in both studies. Increased decline in RBANS of more than 7 points and more than 14 points was detected in the CNP 520 groups versus placebo. A consistent trend in worsening was also observed for CDR-SOB in the CNP520 groups compared to placebo.
- Volumetric MRI (whole brain and hippocampal volume) indicated increased volume loss on active treatment compared to placebo.
- Greater mean weight loss was observed at 26 weeks on CNP520 for both 15 mg and 50 mg doses vs placebo.

The early worsening in some cognitive measures observed with CNP520 appears similar to data reported for other BACE inhibitors.

Taking into consideration the totality of data available, the Sponsors are not confident that a state of equipoise (in which there is a reasonable balance between known and potential benefits and harms) still exists. Therefore, the decision has been made to discontinue assessment of CNP520 in the Generation program.

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[3] In case of a multi-country trial, if the national and global end of trial dates are different in a given Member State, the sponsor shall submit this form two times :

1) At the end of the trial in the individual Member State, section D1.1. shall be completed and submitted to the respective National Competent Authority.

2) At the global end of the trial, the sponsor shall complete section D.2.1. with the global trial end date and the completed form shall be submitted to all participating Member States in order to allow the sponsor to prepare the trial result summary within the 12-months (or 6-months in case of paediatric trials) timeframe.

If the national and global end dates coincide in a concerned Member State, the form shall be submitted only once to the National Competent Authority of this Member State with both sections D1.1. and D2.1 complete.

[4] Cf. Section 4.2. of the detailed guidance CT-1.

D.3.2.2 Number of patients still receiving treatment at time of early termination in the MS concerned by the declaration and their proposed management:

Country	Number of randomized subjects at time of discontinuation *July 11, 2019* (CNP520 or placebo 3:2)
Argentina	0
Australia	**11**
Belgium	**3**
Canada	**37**
Chile	**5**
China	0
Finland	**14**
France	**1**
Germany	0
Iceland	**129**
Israel	**6**
Italy	0
Japan	**28**
Korea, Republic of	**16**
Mexico	**6**
Netherlands	**22**
Portugal	**8**
Singapore	**3**
South Africa	**1**
Spain	**37**
Switzerland	**11**
Taiwan	**3**
United Kingdom	**158**
United States	**646**
Total	**1145**

D.3.2.3 The consequences of early termination for the evaluation of the results and for overall risk benefit assessment of the investigational medicinal product.

At the time of early termination of Study CCNP520A2202J is not available for evaluation. Study results will be further evaluated at the completion of the follow-up phase of the study and a study report will be provided to Health Authorities.

E SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

E.1 I hereby ~~confirm that~~/confirm on behalf of the sponsor that (delete which is not applicable):

- The above information given on this declaration is correct; and
- That the clinical trial summary report will be submitted within the applicable deadlines in accordance with the applicable guidance by the Commission.[5]

E.2	**APPLICANT TO THE COMPETENT AUTHORITY** (as stated in C.1)	☒
E.2.1	Date : 07-Aug-2020	
E.2.2	Signature : 5.1.2.e [redacted]	
E.2.3	Print name: 5.1.2.e [redacted], on behalf of 5.1.2.e [redacted]	

E.3	**APPLICANT TO THE ETHICS COMMITTEE** (as stated in C.2) **:**	☐
E.3.1	Date :	
E.3.2	Signature :	
E.3.3	Print name:	

[5] Section 4.3. of the detailed guidance CT-1.