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Attn. Competent Authority
Parnassusplein 5
2511 VX Den Haag,
The Netherlands

Bucharest, Date: 26 July 2021

Subject:	**Declaration of the end of trial - Early termination**
EudraCT no.:	2018-004233-33
Novartis study no.:	CMHS552A12101
ToetsingOnline Dossier no.:	**NL71107.056.19**
Study title:	A first-in-human, randomized, subject-blinded, placebo-controlled, single ascending dose study to investigate the safety, tolerability and pharmacokinetics of MHS552 in healthy volunteers

Dear Madam, dear Sir,

On behalf of the Sponsor, **Novartis Pharma AG**, Parexel International Romania s.r.l. herewith notifies the global end of the clinical trial.

This is a premature early termination of the trial.

On 07-May-2021, the CMHS552A12101 study was placed on temporary halt after two subjects in the last two cohorts (one in B2/8 mg and one in B3/15 mg) developed CTCAE Grade 2 hypersensitivity-like reactions, i.e., skin rash, thereby meeting one of the study's pre-specified stopping rules. In addition, one of these subjects later developed a Serious Adverse Event (SAE) of renal insufficiency. Both subjects have completely recovered.
The temporary halt notification was submitted to CCMO on 10-May-2021 and approved on 28-May-2021.
Since the temporary halt was initiated, no further enrollment occurred, but previously treated subjects completed their follow-up visits.

A safety review has been conducted for the study including the 60 subjects enrolled up until the time of the temporary halt. Originally, 64 subjects had been planned (without optional cohorts) and at the time of the halt, 7 out of 8 subjects had completed Cohort B2 and 5 out of 8 subjects had completed Cohort B3. After the safety review, it was determined that sufficient information on MHS552 including reaching a maximum tolerable dose

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(MTD) was achieved and therefore it would not be necessary to request approval to reopen the study to test additional subjects.
Therefore, the study is terminated early and interim data from the FIH study shows a generally favorable safety and tolerability profile for MHS552 up to 90 ug/kg i.v. or 8 mg s.c. doses.
The data from this FIH study including the pharmacokinetics, pharmacodynamics, and safety results will be used to determine the dose and design for the next study, and the overall risk benefit assessment remains favorable for the continued development of MHS552.

The end of trial was achieved in The Netherlands (and globally) on 19-July-2021.

For Netherlands, the results of this clinical trial will be submitted within the applicable timeline as a separate submission of the clinical trial report (summary) to fulfill national reporting obligations.

Please find the following study documents supporting this notification attached to this e-mail:

CCMO numbering	Document	Version/Date
A1	Cover letter	26-Jul-2021
B7	Declaration of the end of trial form	26-Jul-2021

With this submission, we declare that all relevant documents in the present submission dossier are signed by the persons authorized for this task.

We trust that the information provided in the application is sufficient, however if you require any further information, please contact us.

Yours faithfully,

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