**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**

*For official use:*

| | | |
|---|---|---|
| Date of receiving the request: | Date of request for additional information: | Grounds for non acceptance / negative opinion : |
| Date of request for information to make it valid: | | Give date: |
| Date of valid application : | Date of receipt of additional / amended information : | Authorisation / positive opinion: |
| Date of start of procedure : | | Give date: |
| Competent authority registration number : | | Withdrawal of application : |
| Ethics Committee registration number : | | Give date : |

## A: Trial identification

**A1. National Competent Authority:**

UK - MHRA

**A2. European Clinical Trials Database (EudraCT) number:**

2021-000672-11

**A3. Full title of the trial:**

A Phase 2a, Open-Label Study to Evaluate the Safety and Efficacy of Selgantolimod (SLGN)-Containing Combination Therapies for the Treatment of Chronic Hepatitis B (CHB)

**A3-1. Title of the trial for lay people, in easily understood, i.e. non-technical, language**

A study to understand the safety and effectiveness of an investigational drug called Selgantolimod in combination with other drugs for the treatment of long term hepatitis B infection

**A3-2. Name or abbreviated title of the trial where available:**

**A4. Sponsor's protocol:**

Number: GS-US-465-4439
Version: Original
Date: 04/03/2021

**A5-1. ISRCTN number, if available :**

**A5-2. US NCT number:**

**A5-3. Who Universal Trial Reference Number (UTRN)**

**A5-4. Other Identifiers:**

| Name | Identifier |
|---|---|

**A6. Is this a resubmission?**

○ Yes ◉ No

**A7. Is the trial part of a Paediatric Investigation Plan?**

○ Yes ◉ No ○ Not Answered

## B: Identification of the sponsor responsible for the request

**B1. Sponsor**

**SP1**
**Contact person**

| | |
|---|---|
| Name of organisation | Gilead Sciences, Inc. |
| Given name | PPD |
| Family name | PPD |
| Address | 333 Lakeside Drive |
| Town/city | Foster City |
| Post code | CA 94404 |
| Country | United States |
| Telephone | PPD |
| Fax | PPD |
| E-mail | PPD |

**B2.Legal Representative for the purpose of this CTIMP.**
*A legal representative must be appointed for a clinical trial of an investigational medicinal product (CTIMP) if the sponsor is not established in the UK or on the MHRA approved country list (please refer to question specific guidance).*

**Legal Representative 1**

**Contact person**

| | |
|---|---|
| Name of organisation | Gilead Sciences Ltd |
| Given name | PPD |
| Family name | PPD |

| | |
|---|---|
| Address | 280 High Holborn |
| Town/city | London |
| Post code | WC1V 7EE |
| Country | United Kingdom |
| Telephone | PPD |
| Fax | PPD |
| E-mail | PPD |

**B3. Status of the sponsor:** Commercial

**B.4 Source(s) of Monetary or Material Support for the clinical trial (repeat as necessary):**

| | |
|---|---|
| Name of organisation | Gilead Sciences, Inc. |
| Country | United States |

**B.5 Contact point designated by the sponsor for further information on the trial:**

| | |
|---|---|
| Name of organisation | Gilead Sciences International Ltd. |
| Functional name of contact point | Clinical trials mailbox |
| Street Address | Flowers Building, Granta Park |
| Town/city | Abington, Cambridge |
| Post code | CB21 6GT |
| Country | United Kingdom |
| Telephone | +44 1223 897284 |
| Fax | |
| E-mail | clinical.trials@gilead.com |

## C: Applicant identification

### C1. Request for the competent authority

**C1-1. Who is responsible for the Clinical Trial Authorisation Application?**

Sponsor

**C1-4. Complete the details of the applicant below even if they are provided elsewhere on the form:**

**Contact person**

Person or organisation name: Gilead Science Ltd

Contact person Given name PPD

| | |
|---|---|
| Contact person Family name | PPD |
| Address | 280 High Holborn |
| Town/city | London |
| Post code | WC1V 7EE |
| Country | United Kingdom |
| Telephone | PPD |
| Fax | PPD |
| E-mail | PPD |

**C1-5. Do you want a xml file copy of the CTA form data saved on EudraCT?**

(•) Yes ( ) No ( ) Not Answered

**Provide the e-mail address(es) to which it should be sent**

*These email addresses must have Eudralink accounts for secure password protected delivery unless you answer No to question below.*

**E-mail address**

PPD

PPD

**Do you want to receive this via password protected links?**

( ) Yes (•) No ( ) Not Answered

*You must have a EudraLink account to receive via password protected link. If you do not know if you have a EudraLink account, answer no above and the .xml file will be transmitted by less secure e-mail link(s).*

## C2.Request for ethics commitee

**C2-1. Who is responsible for the Clinical Trial Authorisation Application?**

.....

**C2-5. Complete the details of the applicant below even if they are provided elsewhere on the form**

| | |
|---|---|
| Person or organisation name: | ..... |
| Title: | ..... |
| Forename/Initials: | ..... |
| Surname: | ..... |
| Middlename: | ..... |
| Address: | ..... |
| Town/city: | ..... |
| Post code: | ..... |
| Country: | ..... |
| Telephone: | ..... |
| Fax: | ..... |
| E-mail: | ..... |

## Part D: Investigational Medicinal Products

**D: Information on the IMPs**

***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, if applicable. If the trial is performed with several products please create a separate set of the following questions for each product. If the product is a combination product please give separate information for each active substance.***

***Click on the first row and enter details of the product in the following screens. When you have completed the details, click on the navigate button or the "See All" link and return to this section to enter details of the next product. When you have completed details of all products please move to question D7 using the navigation screen.***

**D. Investigational medicinal products**

**PR1** Selgantolimod

**PR2** Vemlidy® (tenofovir alafenamide)

**PR3** Opdivo® (Nivolumab)

**PR4** VIR-2218

**D1. Indicate which of the following is described below then repeat as necessary for each:**

This refers to the IMP number: **PR1**
Investigational medicinal product category:
Test IMP

**D2. Status of the IMP** ***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***

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

◯ Yes ◉ No ◯ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?
◯ Yes ◉ No ◯ Not Answered

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?
◯ Yes ◉ No ◯ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group
◯ Yes ◉ No ◯ Not Answered

Other :
◯ Yes ◉ No ◯ Not Answered

**D2-3. IMPD submitted:**

Full IMPD
◉ Yes ○ No ○ Not Answered

Simplified IMPD
○ Yes ◉ No ○ Not Answered

*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only
○ Yes ◉ No ○ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

○ Yes ◉ No ○ Not Answered

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

○ Yes ◉ No ○ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

○ Yes ◉ No ○ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?
○ Yes ◉ No ○ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?
○ Yes ◉ No ○ Not Answered

**This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".**

## D3. Description of IMP

**D3-1.**

| | |
|---|---|
| D.3.1 Product name where applicable | Selgantolimod |
| D.3.2 Product code where applicable | GS-9688 |
| D.3.3 ATC codes, if officially registered | |
| D.3.4 Pharmaceutical form (use standard terms) | Tablet |

| | |
|---|---|
| D.3.4.1 Is this a specific paediatric formulation? | ◯ Yes ◉ No ◯ Not Answered |
| D.3.5 Maximum duration of treatment of a subject according to the protocol | once a week for up to 24 weeks |

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ◯ per day ◯ total ◯ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed

D.3.6.2 Specify per day or total ◉ per day ◯ total ◯ Not Answered

D.3.6.2 Specify total dose (number and unit) [redacted] mg milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Oral use

**D.3.7 Routes of administration for this IMP**

Oral use

**This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".**

**D3-8. Active substances**

*Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.*

**Active Substance 1**

| | |
|---|---|
| Name of active substance (INN or proposed INN if available): | Selgantolimod |
| CAS number: | 2004677-13-6 |
| Current sponsor code: | GS-9688 |
| Other descriptive name: | SLGN |
| Full Molecular formula | |
| Chemical/biological description of the Active Substance | Selgantolimod (SLGN, also GS-9688) is a TLR8 agonist that induces the cellular immune mediator interleukin (IL)-12 and the antiviral cytokines tumor necrosis factor (TNF)-α and interferon (IFN)-γ in vitro in peripheral blood mononuclear cells (PBMCs). |

*Strength*

| | |
|---|---|
| Concentration unit: | mg milligram(s) |
| Concentration type: | equal |
| Concentration number (only use both fields for range): | [redacted] |

**D3-11. Type of IMP**

Does the IMP contain an active substance:

| | |
|---|---|
| Of chemical origin? | (●) Yes ( ) No ( ) Not Answered |
| Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) | ( ) Yes (●) No ( ) Not Answered |
| *Is this a:* | |
| Advanced Therapy IMP (ATIMP) [1] | ( ) Yes (●) No ( ) Not Answered |
| Combination product that includes a device, but does not involve an Advanced Therapy | ( ) Yes (●) No ( ) Not Answered |
| Radiopharmaceutical medicinal product? | ( ) Yes (●) No ( ) Not Answered |
| Immunological medicinal product (e.g. vaccine, allergen, immune serum)? | ( ) Yes (●) No ( ) Not Answered |
| Plasma derived medicinal product? | ( ) Yes (●) No ( ) Not Answered |
| Extractive medicinal product? | ( ) Yes (●) No ( ) Not Answered |
| Recombinant medicinal product? | ( ) Yes (●) No ( ) Not Answered |
| Medicinal product containing genetically modified organisms? | ( ) Yes (●) No ( ) Not Answered |
| Herbal medicinal product? | ( ) Yes (●) No ( ) Not Answered |
| Homeopathic medicinal product? | ( ) Yes (●) No ( ) Not Answered |
| Another type of medicinal product? | ( ) Yes (●) No ( ) Not Answered |

Specify the mode of action for the active substance in this medicinal product
*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.* TLR8 agonist

Is it an IMP to be used in a first-in-human clinical trial? ( ) Yes (●) No ( ) Not Answered

*[1,2,3,4,5] Complete sections D.4, D.5, D.6. and D.7, as applicable*
*[2,3] As defined in Annex 1 part IV of Directive 2001/83/EC as amended*
*[4] As defined in Article 2(1)(b) of Regulation 1394/2007/EC*
*[6] Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007*

**D1. Indicate which of the following is described below then repeat as necessary for each:**

This refers to the IMP number: **PR2**
Investigational medicinal product category:
Test IMP

**D2. Status of the IMP** ***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***

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

◉ Yes ○ No ○ Not Answered

Trade name:
Vemlidy® (tenofovir alafenamide)
EV Product Code
Name of the MA holder:
Gilead Sciences Ireland UC
MA number (if MA granted by a Member State):
EU/1/16/1154/001, EU/1/16/1154/002
Is the IMP modified in relation to its MA?
○ Yes ◉ No ○ Not Answered

Which country granted the MA?
European Union
Is this the Member State concerned with this application?
◉ Yes ○ No ○ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?
○ Yes ◉ No ○ Not Answered

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?
○ Yes ◉ No ○ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group
○ Yes ◉ No ○ Not Answered

Other :
○ Yes ○ No ◉ Not Answered

**D2-3. IMPD submitted:**

Full IMPD
○ Yes ◉ No ○ Not Answered

Simplified IMPD
○ Yes ◉ No ○ Not Answered

*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only

(●) Yes ( ) No ( ) Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

(●) Yes ( ) No ( ) Not Answered

Specify which Member States:

CCI

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

( ) Yes (●) No ( ) Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

( ) Yes (●) No ( ) Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

( ) Yes (●) No ( ) Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

( ) Yes (●) No ( ) Not Answered

**This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".**

## D3. Description of IMP

**D3-1.**

| | |
|---|---|
| D.3.1 Product name where applicable | Vemlidy® (tenofovir alafenamide) |
| D.3.2 Product code where applicable | |

| | |
|---|---|
| D.3.3 ATC codes, if officially registered | J05AF13 |
| D.3.4 Pharmaceutical form (use standard terms) | Film-coated tablet |
| D.3.4.1 Is this a specific paediatric formulation? | ◯ Yes ◉ No ◯ Not Answered |
| D.3.5 Maximum duration of treatment of a subject according to the protocol | up to 84 weeks |

**D.3.6 Dose allowed**

| | |
|---|---|
| D.3.6.1 First dose for first-in-human clinical trial | |
| D.3.6.1 Specify per day or total: | ◯ per day ◯ total ◯ Not Answered |
| D.3.6.1 Specify total dose (number and unit) | |
| D.3.6.1 Route of administration (relevant to the first dose): | |
| D.3.6.2 Maximum dose allowed | |
| D.3.6.2 Specify per day or total | ◉ per day ◯ total ◯ Not Answered |
| D.3.6.2 Specify total dose (number and unit) | CCI mg milligram(s) |
| D.3.6.2 Route of administration (relevant to the maximum dose): | Oral use |

**D.3.7 Routes of administration for this IMP**

Oral use

**This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".**

**D3-8. Active substances**

*Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.*

**Active Substance 1**

| | |
|---|---|
| Name of active substance (INN or proposed INN if available): | TENOFOVIR ALAFENAMIDE |
| CAS number: | 379270-37-8 |
| Current sponsor code: | GS-7340 |
| Other descriptive name: | TAF |
| Full Molecular formula | |
| Chemical/biological description of the Active Substance | This is an antiviral medicine, known as a nucleotide reverse transcriptase inhibitor (NtRTI). |
| *Strength* | |
| Concentration unit: | mg milligram(s) |

| | |
|---|---|
| Concentration type: | equal |
| Concentration number (only use both fields for range): | [redacted] |

**D3-11. Type of IMP**

Does the IMP contain an active substance:

| | | | |
|---|---|---|---|
| Of chemical origin? | ◉ Yes | ○ No | ○ Not Answered |
| Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) | ○ Yes | ◉ No | ○ Not Answered |
| *Is this a:* | | | |
| Advanced Therapy IMP (ATIMP) (1) | ○ Yes | ◉ No | ○ Not Answered |
| Combination product that includes a device, but does not involve an Advanced Therapy | ○ Yes | ◉ No | ○ Not Answered |
| Radiopharmaceutical medicinal product? | ○ Yes | ◉ No | ○ Not Answered |
| Immunological medicinal product (e.g. vaccine, allergen, immune serum)? | ○ Yes | ◉ No | ○ Not Answered |
| Plasma derived medicinal product? | ○ Yes | ◉ No | ○ Not Answered |
| Extractive medicinal product? | ○ Yes | ◉ No | ○ Not Answered |
| Recombinant medicinal product? | ○ Yes | ◉ No | ○ Not Answered |
| Medicinal product containing genetically modified organisms? | ○ Yes | ◉ No | ○ Not Answered |
| Herbal medicinal product? | ○ Yes | ◉ No | ○ Not Answered |
| Homeopathic medicinal product? | ○ Yes | ◉ No | ○ Not Answered |
| Another type of medicinal product? | ○ Yes | ◉ No | ○ Not Answered |

Specify the mode of action for the active substance in this medicinal product
*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.* Tenofovir alafenamide is a phosphonamidate prodrug of tenofovir (2' deoxyadenosine monophosphate analogue). Tenofovir diphosphate inhibits HBV replication through incorporation into viral DNA by the HBV reverse transcriptase, which results in DNA chain termination.

| | | | |
|---|---|---|---|
| Is it an IMP to be used in a first-in-human clinical trial? | ○ Yes | ◉ No | ○ Not Answered |

*(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable*
*(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended*
*(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC*
*(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007*

**D1. Indicate which of the following is described below then repeat as necessary for each:**

This refers to the IMP number: **PR3**
Investigational medicinal product category:
Test IMP

**D2. Status of the IMP** ***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***

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

◉ Yes ○ No ○ Not Answered

Trade name:
Opdivo® (Nivolumab)
EV Product Code
Name of the MA holder:
Bristol-Myers Squibb Pharma EEIG
MA number (if MA granted by a Member State):
EU/1/15/1014/001
Is the IMP modified in relation to its MA?
○ Yes ◉ No ○ Not Answered

Which country granted the MA?
European Union
Is this the Member State concerned with this application?
◉ Yes ○ No ○ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?
○ Yes ◉ No ○ Not Answered

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?
○ Yes ◉ No ○ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group
○ Yes ◉ No ○ Not Answered

Other :
○ Yes ◉ No ○ Not Answered

**D2-3. IMPD submitted:**

Full IMPD
○ Yes ◉ No ○ Not Answered

Simplified IMPD
○ Yes ◉ No ○ Not Answered
*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only

◉ Yes ○ No ○ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

◉ Yes ○ No ○ Not Answered

Specify which Member States:


**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

○ Yes ◉ No ○ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

○ Yes ◉ No ○ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

○ Yes ◉ No ○ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

○ Yes ◉ No ○ Not Answered

**This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".**

## D3. Description of IMP

**D3-1.**

| | |
|---|---|
| D.3.1 Product name where applicable | Opdivo® (Nivolumab) |
| D.3.2 Product code where applicable | |

| | |
|---|---|
| D.3.3 ATC codes, if officially registered | L01XC17 |
| D.3.4 Pharmaceutical form (use standard terms) | Concentrate for solution for infusion |
| D.3.4.1 Is this a specific paediatric formulation? | ◯ Yes ◉ No ◯ Not Answered |
| D.3.5 Maximum duration of treatment of a subject according to the protocol | every 4 weeks for 24 weeks |

**D.3.6 Dose allowed**

| | |
|---|---|
| D.3.6.1 First dose for first-in-human clinical trial | |
| D.3.6.1 Specify per day or total: | ◯ per day ◯ total ◯ Not Answered |
| D.3.6.1 Specify total dose (number and unit) | |
| D.3.6.1 Route of administration (relevant to the first dose): | |

| | |
|---|---|
| D.3.6.2 Maximum dose allowed | |
| D.3.6.2 Specify per day or total | ◉ per day ◯ total ◯ Not Answered |
| D.3.6.2 Specify total dose (number and unit) | CCI mg/kg milligram(s)/kilogram |
| D.3.6.2 Route of administration (relevant to the maximum dose): | Intravenous use |

**D.3.7 Routes of administration for this IMP**

Intravenous use

**This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".**

**D3-8. Active substances**

*Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.*

**Active Substance 1**

| | |
|---|---|
| Name of active substance (INN or proposed INN if available): | Nivolumab |
| CAS number: | |
| Current sponsor code: | |
| Other descriptive name: | |
| Full Molecular formula | |
| Chemical/biological description of the Active Substance | an anti-PD-1 immunoglobulin (Ig)G4 monoclonal antibody |
| *Strength* | |
| Concentration unit: | mg/ml milligram(s)/millilitre |

| | |
|---|---|
| Concentration type: | equal |
| Concentration number (only use both fields for range): | [redacted] |

**D3-11. Type of IMP**

Does the IMP contain an active substance:

| | |
|---|---|
| Of chemical origin? | ○ Yes ◉ No ○ Not Answered |
| Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) | ◉ Yes ○ No ○ Not Answered |
| *Is this a:* | |
| Advanced Therapy IMP (ATIMP) (1) | ○ Yes ◉ No ○ Not Answered |
| Combination product that includes a device, but does not involve an Advanced Therapy | ○ Yes ◉ No ○ Not Answered |
| Radiopharmaceutical medicinal product? | ○ Yes ◉ No ○ Not Answered |
| Immunological medicinal product (e.g. vaccine, allergen, immune serum)? | ○ Yes ◉ No ○ Not Answered |
| Plasma derived medicinal product? | ○ Yes ◉ No ○ Not Answered |
| Extractive medicinal product? | ○ Yes ◉ No ○ Not Answered |
| Recombinant medicinal product? | ◉ Yes ○ No ○ Not Answered |
| Medicinal product containing genetically modified organisms? | ○ Yes ◉ No ○ Not Answered |
| Herbal medicinal product? | ○ Yes ◉ No ○ Not Answered |
| Homeopathic medicinal product? | ○ Yes ◉ No ○ Not Answered |
| Another type of medicinal product? | ○ Yes ◉ No ○ Not Answered |

Specify the mode of action for the active substance in this medicinal product
*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.* Nivolumab is a human immunoglobulin G4 (IgG4) monoclonal antibody (HuMAb), which binds to the programmed death-1 (PD-1) receptor and blocks interaction with PD-L1 and PD-L2.

Is it an IMP to be used in a first-in-human clinical trial? ○ Yes ◉ No ○ Not Answered

*(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable*
*(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended*
*(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC*
*(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007*

**D1. Indicate which of the following is described below then repeat as necessary for each:**

This refers to the IMP number: **PR4**
Investigational medicinal product category:
Test IMP

**D2. Status of the IMP** ***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***

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

○ Yes ◉ No ○ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?
○ Yes ◉ No ○ Not Answered

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?
○ Yes ◉ No ○ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group
○ Yes ◉ No ○ Not Answered

Other :
○ Yes ○ No ◉ Not Answered

**D2-3. IMPD submitted:**

Full IMPD
◉ Yes ○ No ○ Not Answered

Simplified IMPD
○ Yes ◉ No ○ Not Answered

*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only
○ Yes ◉ No ○ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

○ Yes ◉ No ○ Not Answered

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

○ Yes ◉ No ○ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

◯ Yes ◉ No ◯ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

◯ Yes ◉ No ◯ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

◯ Yes ◉ No ◯ Not Answered

**This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".**

## D3. Description of IMP

**D3-1.**

| | |
|---|---|
| D.3.1 Product name where applicable | VIR-2218 |
| D.3.2 Product code where applicable | |
| D.3.3 ATC codes, if officially registered | |
| D.3.4 Pharmaceutical form (use standard terms) | Solution for injection |
| D.3.4.1 Is this a specific paediatric formulation? | ◯ Yes ◉ No ◯ Not Answered |
| D.3.5 Maximum duration of treatment of a subject according to the protocol | once every 4 weeks for 24 weeks |

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ◯ per day ◯ total ◯ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed

D.3.6.2 Specify per day or total ◉ per day ◯ total ◯ Not Answered

D.3.6.2 Specify total dose (number and unit) CCI mg milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Subcutaneous use

**D.3.7 Routes of administration for this IMP**

Subcutaneous use

**This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".**

**D3-8. Active substances**

*Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.*

**Active Substance 1**

| | |
|---|---|
| Name of active substance (INN or proposed INN if available): | |
| CAS number: | |
| Current sponsor code: | VIR-2218 |
| Other descriptive name: | ALN-HBV-02 (drug product); ALN-81890 (drug substance); AD-81890 (drug substance laboratory code). |
| Full Molecular formula | |
| Chemical/biological description of the Active Substance | ALN-81890 is a chemically synthesized double stranded oligonucleotide covalently linked to a ligand containing three N-acetylgalactosamine (GalNAc) residues. |

*Strength*

| | |
|---|---|
| Concentration unit: | mg/ml milligram(s)/millilitre |
| Concentration type: | equal |
| Concentration number (only use both fields for range): | CCI |

**D3-11. Type of IMP**

Does the IMP contain an active substance:

| | | | |
|---|---|---|---|
| Of chemical origin? | ◉ Yes | ○ No | ○ Not Answered |
| Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) | ○ Yes | ◉ No | ○ Not Answered |

*Is this a:*

| | | | |
|---|---|---|---|
| Advanced Therapy IMP (ATIMP) [1] | ○ Yes | ◉ No | ○ Not Answered |
| Combination product that includes a device, but does not involve an Advanced Therapy | ○ Yes | ◉ No | ○ Not Answered |
| Radiopharmaceutical medicinal product? | ○ Yes | ◉ No | ○ Not Answered |
| Immunological medicinal product (e.g. vaccine, allergen, immune serum)? | ○ Yes | ◉ No | ○ Not Answered |
| Plasma derived medicinal product? | ○ Yes | ◉ No | ○ Not Answered |
| Extractive medicinal product? | ○ Yes | ◉ No | ○ Not Answered |
| Recombinant medicinal product? | ○ Yes | ◉ No | ○ Not Answered |
| Medicinal product containing genetically modified organisms? | ○ Yes | ◉ No | ○ Not Answered |
| Herbal medicinal product? | ○ Yes | ◉ No | ○ Not Answered |

| | |
|---|---|
| Homeopathic medicinal product? | ◯ Yes ◉ No ◯ Not Answered |
| Another type of medicinal product? | ◯ Yes ◉ No ◯ Not Answered |

Specify the mode of action for the active substance in this medicinal product
*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.* Ribonucleic acid interference (RNAi) therapeutic silencing HBV RNAs

| | |
|---|---|
| Is it an IMP to be used in a first-in-human clinical trial? | ◯ Yes ◉ No ◯ Not Answered |

*(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable*
*(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended*
*(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC*
*(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007*

## D8. Information on placebo *(if relevant; repeat as necessary)*

**D8. Is there a placebo:**

◯ Yes ◉ No ◯ Not Answered

## D9. Sites responsible for final QP release for distribution to investigators.

**D9-1. IMPs and placebos for which no responsible site needs to be identified.**

This section is used to identify IMPs and placebos which:

- Have an MA in the EU **and**
- Are sourced from the EU market **and**
- Are used in the trial without modification (eg not overencapsulated) **and**
- The packaging and labeling is carried out for local use only as per article 9.2 of the Directive 2005/28/EC (GCP Directive).

*If all the conditions above are met, then select below the IMPs and placebos to which this applies.*

## Index of Sites where the qualified person certifies batch release

*In accordance with paragraph 38 of Annex 13 of Volume 4 of the Rules Governing Medicinal Products in the European Union*

**D9-2. Who is responsible in the Community for the certification of the finished IMP or placebo?**
*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 D1 or D7 In the case of multiple sites indicate the product certified by each site.*

**RS1**

Importer

Name of the organisation: CCI [redacted]
Address CCI [redacted]
Town/city CCI [redacted]
Post code
Country CCI [redacted]

Give the manufacturing authorisation number

CCI [redacted]

If no authorisation, give the reasons:

*Select the relevant IMP(s) and Placebo(s) from the drop down lists.*

IMP
PR1

IMP
PR2

IMP
PR3

IMP
PR4

## E: Design of the Trial.

### E.1 Medical Condition or Disease under Investigation

**E1-1. Medical condition or disease under investigation (1)**

Specify the medical condition(s) to be investigated (free text) :
Chronic Hepatitis B (CHB)

Medical condition in easily understood language
Long term infection with hepatitis B virus

Identify the therapeutic area
Diseases [C] - Virus Diseases [C02]

*(1) In the case of healthy volunteer trials, the intended indication for the product under development should be provided.*

**E1-2. MedDRA information (2)**

**MR1**

| | |
|---|---|
| Version | 20.1 |
| Level | PT |
| Classification Code | 10008910 |
| Term | Chronic hepatitis B |
| SOC | 10021881 - Infections and infestations |

*(2) Applicants are encouraged to provide the MedDRA lower level term (LLT) if applicable and classification code.*

**E1-3. Is any of the conditions being studied a rare disease? (3)**

◯ Yes ◉ No ◯ Not Answered

*(3) Refer to "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/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/09/WC500003773.pd*

### E2. Objective of the trial

**E2-1. What is the principal research question/objective?** *Please put this in language comprehensible to a lay person.*

- To evaluate the safety and tolerability of study treatment(s)
- To evaluate the efficacy of study treatment(s) as measured by the proportion of subjects who achieve functional cure, defined as HBsAg loss and HBV DNA < 20 IU/mL at FU Week 24

**E2-2. What are the secondary research questions/objectives if applicable?** *Please put this in language comprehensible to a lay person.*

- To evaluate the proportion of subjects with HBsAg loss with and without anti-HBsAg seroconversion during the study
- To evaluate in subjects with CHB who are hepatitis B e antigen (HBeAg)-positive at baseline, the proportion of subjects who achieve HBeAg loss with and without anti-HBeAg seroconversion during the study
- To evaluate the proportion of subjects who remain off NUC treatment during FU
- To evaluate the proportion of subjects experiencing HBV virologic breakthrough (defined as HBV DNA ≥ 69 IU/mL for 2 consecutive visits after having been < 20 IU/mL OR confirmed HBV DNA ≥ 1 log10 IU/mL increase from nadir on treatment) during study treatment(s)

**E2-3. Is there a sub-study?**

(●) Yes ( ) No ( ) Not Answered

Give the full title, date and version of each sub-study and their related objectives:

Optional Intensive Pharmacokinetic Substudy (separate consent required).
Subjects who are willing to consent will be eligible to participate in the optional PK substudy for an intensive serial PK sample collection to expand our knowledge and understanding of SLGN and VIR-2218 PK in CHB-infected subjects. If a subject chooses to participate in this substudy, intensive PK blood samples will be collected as described below instead of the sparse plasma PK samples for that specific analyte on that specific visit.

For VIR-2218 and metabolite PK evaluation
Serial PK blood samples will be collected on Day 1 and at Week 20 in-clinic treatment visits in Cohorts 1, 2 (Group A), and 3 relative to VIR- 2218 dosing in clinic on the morning of intensive PK visit at the time points listed below:
- Predose, 0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 8, 10, 12, and 24 hours postdose (8, 10, and 12 hour collections are optional)

For SLGN PK evaluation
Serial PK blood samples will be collected at any one in-clinic treatment visit between Weeks 20 through 32 (in Cohorts 1 and 2 [Group A]) and Weeks 12 through 20 (in Cohorts 2 [Group B], and 3) relative to SLGN dosing in clinic on the morning of intensive PK visit at the time points
listed below:
- Predose, 0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 8, 10, 12, and 24 hours postdose (8, 10, and 12 hour collections are optional)

Pharmacogenomic Research:
All subjects who are willing to provide separate written consent will be eligible to participate in the PG research. This PG blood sample should be drawn at the Baseline/Day 1 visit. However, if the sample is not obtained at Baseline/Day 1 visit the sample may then be drawn at any time during the study. The sample will be stored, for future PG analysis.

Samples for Optional Future Research:
Subjects will be requested to consent to allow for the use of the remainder of their already collected specimens for optional future research.

**E3. Please list the principal inclusion criteria (list the most important, max 5000 characters).**

1. Must have the ability to understand and sign a written informed consent form (ICF), which must be obtained prior to initiation of study procedures
2. Adult male and nonpregnant, nonlactating female subjects, 18 to 65 years (19-65 years of age in Republic of Korea) of age inclusive based on the date of the screening visit
3. Documented evidence of chronic HBV infection (eg, HBsAg positive for more than 6 months) with detectable HBsAg levels (> 1.5 log10 IU/mL) at screening
4. Screening electrocardiogram (ECG) without clinically significant abnormalities and with QTcF interval (QT corrected using Fridericia's formula) ≤ 450 msec for males and ≤ 470 msec for females.
5. Females of childbearing potential (as defined in Appendix 4 of the protocol must have a negative serum pregnancy test at screening and a negative urine pregnancy test at baseline prior to enrollment
6. Male and female subjects of childbearing potential who engage in heterosexual intercourse must agree to use protocol-specified method(s) of contraception as described in Appendix 4 of the protocol. Must be willing and able to comply with all study requirements.

Subjects in Cohort 1 should meet the following additional criteria to be eligible to participate in this study:
7. Have been on a commercially available HBV NUC treatment(s) (ie, TAF, TDF, entecavir, adefovir, lamivudine, telbivudine, either as single agents or in combination) with no change in regimen for 3 months prior to screening and

willing to initiate TAF 25 mg.
8. Have a historic HBV DNA < 69 IU/mL, measured at least once at local laboratory, 6 or more months prior to screening.
9. HBV DNA < 20 IU/mL by central laboratory at screening

Subjects in Cohort 2 and 3 should meet the following additional criteria at screening to be eligible to participate in this study:
10. HBV DNA > 2000 IU/mL (HBeAg-negative) and HBV DNA > 20,000 IU/mL (HBeAgpositive)

**E4. Please list the principal exclusion criteria (list the most important, max 5000 characters).**

1. Extensive bridging fibrosis or cirrhosis as defined clinically by any 1 of the following:
a) Metavir ≥ 3 or Ishak fibrosis score ≥ 4 by a liver biopsy within 3 years of screening, or, in the absence of an appropriate liver biopsy, either:
b) Screening FibroTest score of > 0.48 and AST to platelet ratio index (APRI) > 1 by central laboratory, or
c) Historic FibroScan with a result > 9 kPa within ≤ 1 year of screening
If liver biopsy is available, the liver biopsy result supersedes (b) and/or (c, if available)
If an appropriate liver biopsy is not available, fibrosis will be evaluated by (b) and/or (c, if available). In the event of discordance between (b) and (c), the FibroScan results will take precedence.
2. Subjects meeting any of the following laboratory parameters at screening:
a) Hemoglobin < 12 g/dL (for males) or < 11 g/dL (for females)
b) White blood cell (WBC) count < 2500 cells/mm3
c) Neutrophil count < 1500 cell/mm3 (or < 1000 cell/mm3 if considered a physiological variant in a subject of African descent)
d) ALT ≥ 2 x ULN (Cohort 1 only), ALT > 5 x ULN (Cohorts 2 and 3)
e) International normalized ratio (INR) > ULN unless the subject is stable on ananticoagulant regimen affecting INR
f) Albumin < 3.5 g/dL
g) Direct bilirubin > 1.5 x ULN
h) Platelet Count < 100,000/uL
i) Positive autoantibodies, defined as any one or more of the following:
i. Antinuclear antibodies (ANA) > 1:80
ii. Smooth muscle antibodies (anti-SMA) > 1:80
iii. Antimitochondrial antibodies (AMA) > 1:40
iv. Anti-thyroid peroxidase (anti-TPO) > 35 IU/mL
j) Estimated creatinine clearance (CLcr) < 60 mL/min (using the Cockcroft-Gault method) based on serum creatinine and actual body weight as measured at the screening evaluation, ie,
Male: ((140 – Age [years]) x (Weight [kg])) / (72 x (Serum Creatinine [mg/dl])) = CLcr (mL/min)
Female: ((140 – Age [years]) x (Weight [kg])) x 0.85 / (72 x (Serum Creatinine [mg/dL])) = CLcr (mL/min)
3. Subjects in Cohort 2 and 3: Received OAV treatment for HBV within 6 months of screening
4. Co-infection with HIV, HCV, or hepatitis D virus (HDV). Subjects who are HCV Ab or HDV Ab positive, but have a documented negative HCV RNA or HDV RNA, respectively, are eligible.
5. Current or prior history of HCC (eg, as evidenced by prior imaging) or screening α-fetoprotein ≥ 50 ng/mL without imaging to rule out HCC
6. Current or prior history of clinical hepatic decompensation (eg, ascites, encephalopathy, or variceal hemorrhage).
7. Malignancy within 5 years prior to screening, with the exception of specific cancers that are cured by surgical resection (eg, basal cell skin cancer). Subjects under evaluation for possible malignancy are not eligible
8. Significant cardiovascular, ophthalmological, pulmonary, or neurological disease in the opinion of the investigator
9. Diagnosis of any autoimmune disease (eg, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, ulcerative colitis, pneumonitis, autoimmune hepatitis, sarcoidosis, psoriasis of greater than mild severity, autoimmune uveitis, autoimmune nephritis, thyroiditis), poorly controlled diabetes mellitus, significant psychiatric illness, severe chronic obstructive pulmonary disease (COPD), hemoglobinopathy, retinal disease, or are immunosuppressed
10. Chronic liver disease of a non-HBV etiology (eg, Wilson's disease, hemochromatosis, alpha-1-antitrypsin deficiency, cholangitis), except for nonalcoholic fatty liver disease
11. Received solid organ or bone marrow transplant
12. Received prolonged therapy with immunomodulators (eg, corticosteroids) or biologics (eg, monoclonal antibody, interferon, nivolumab) within 6 months of screening
13. Have received inactivated vaccinations (eg, injectable influenza or pneumococcal) within 4 weeks prior to randomization or received live vaccinations within 4 weeks prior to screening
14. Use of another investigational agent within 90 days of screening, unless allowed by the sponsor
15. Current alcohol or substance abuse judged by the investigator to potentially interfere with subject compliance
16. Known hypersensitivity to study drug or formulation excipients
17. Women who are breastfeeding, pregnant, or who wish to become pregnant during the course of the study
18. Female subjects unwilling to refrain from egg donation and in vitro fertilization during and until at least 5 months

after last study drug dose.
19. Male subjects unwilling to refrain from sperm donation during and until at least 5 months after the last study drug dose
20. Use of any prohibited concomitant medications as described in Section 5.3 of the protocol.
21. Believed by the study investigator to be inappropriate for study participation for any reason not otherwise listed.

**E5-1. What is the primary outcome measure for the study?(max 5000 characters)**

The proportion of subjects who achieve functional cure, defined as HBsAg loss and HBV DNA < 20 IU/mL at FU Week 24

**Timepoint(s) of evaluation of this end point (max 800 characters)**
Follow up Week 24

*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.*

**E5-2. Secondary end point(s) (max 5000 characters)**

- The proportion of subjects with HBsAg loss with and without anti-HBsAg seroconversion during the study
- The proportion of subjects with HBeAg loss with and without anti-HBeAg seroconversion during the study in subjects with CHB who are HBeAg-positive at baseline
- The proportion of subjects who remain off NUC treatment during FU
- The proportion of subjects experiencing HBV virologic breakthrough (defined as HBV DNA ≥ 69 IU/mL for 2 consecutive visits after having been < 20 IU/mL or confirmed HBV DNA ≥ 1 log10 IU/mL increase from nadir) during study treatment(s)

**Timepoint(s) of evaluation of this end point (max 800 characters)**
Primary analysis - all subjects within each cohort have completed FU Week 24

**E6. What is the scope of the trial?**

| | | | |
|---|---|---|---|
| Diagnosis | ○ Yes | ◉ No | ○ Not Answered |
| Prophylaxis | ○ Yes | ◉ No | ○ Not Answered |
| Therapy | ○ Yes | ◉ No | ○ Not Answered |
| Safety | ◉ Yes | ○ No | ○ Not Answered |
| Efficacy | ◉ Yes | ○ No | ○ Not Answered |
| Pharmacokinetic | ◉ Yes | ○ No | ○ Not Answered |
| Pharmacodynamic | ◉ Yes | ○ No | ○ Not Answered |
| Bioequivalence | ○ Yes | ◉ No | ○ Not Answered |
| Dose Response | ○ Yes | ◉ No | ○ Not Answered |
| Pharmacogenetic | ○ Yes | ◉ No | ○ Not Answered |
| Pharmacogenomic | ◉ Yes | ○ No | ○ Not Answered |
| Pharmacoeconomic | ○ Yes | ◉ No | ○ Not Answered |
| Others | ○ Yes | ◉ No | ○ Not Answered |

Specify:

**E7-1. Trial type and phase [(1)]**

| | |
|---|---|
| Human pharmacology (Phase I) | ○ Yes ◉ No ○ Not Answered |
| Therapeutic exploratory (Phase II) | ◉ Yes ○ No ○ Not Answered |
| Therapeutic confirmatory (Phase III) | ○ Yes ◉ No ○ Not Answered |
| Therapeutic use (Phase IV) | ○ Yes ◉ No ○ Not Answered |

*(1) 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.*

## E8. Design of the Trial.

**E8-1. Is the trial design controlled?**

○ Yes ◉ No ○ Not Answered

**E8-2. If controlled, specify the comparator:**

| | |
|---|---|
| Other medicinal product(s) | ○ Yes ◉ No ○ Not Answered |
| Placebo | ○ Yes ◉ No ○ Not Answered |
| Other | ○ Yes ◉ No ○ Not Answered |

Number of treatment arms in the trial
4

**E8-3. Single site in the Member State concerned (see also section G):**

○ Yes ◉ No ○ Not Answered

**E8-4. Multiple sites in the Member State concerned (see also section G):**

◉ Yes ○ No ○ Not Answered

Number of sites anticipated in Member State concerned

**E8-5. Multiple Member States**

◉ Yes ○ No ○ Not Answered

Number of sites anticipated in the Community.
4

**E8-6. Trial being conducted both within and outside the EEA**

◉ Yes ○ No ○ Not Answered

Trial conducted completely outside EEA

○ Yes ◉ No ○ Not Answered

Specify the countries in which trial sites are planned

Australia

Denmark

Hong Kong

Korea, Democratic People's Republic of

New Zealand

Singapore

Thailand

United Kingdom

Specify the number of sites anticipated outside of the EEA
26

**E8-7. Will a data monitoring committee (DMC) be convened?**

◯ Yes ◉ No ◯ Not Answered

**E8-8.**

**Definition of the end of trial, and justification in the case where it is not the last visit of the last subject undergoing the trial.**
*If it is the last visit of the last subject, please enter "LVLS". If it is not LVLS provide the definition.*
LVLS

**E8-9. How long do you expect the study to last?** (1)

In all countries concerned by the trial
Years: 3 Months: 0 Days: 0

In the MS concerned
Years: 3 Months: 0 Days: 0

(1) *From the first inclusion until the last visit of the last subject.*

**E8-10. Recruitment start date**

Recruitment start date in MS
01/11/2021
In any country
26/08/2021

(1) *If not provided in the protocol.*

## F: Population of Trial Subjects

**F1. What is the age span of the trial subjects?**

| | | |
|---|---|---|
| Less than 18 years | ○ Yes ◉ No ○ Not Answered | Approx no of participants: 0 |
| Adult (18-64 years) | ◉ Yes ○ No ○ Not Answered | Approx no of participants: 115 |
| Elderly (geater than 65 years) | ◉ Yes ○ No ○ Not Answered | Approx no of participants: 5 |

*The number of participants 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.*

**F2. What is the gender of the trial subjects?**

| | |
|---|---|
| Female | ◉ Yes ○ No ○ Not Answered |
| Male | ◉ Yes ○ No ○ Not Answered |

**F3. Please select the categories of the trial subjects:**

| | |
|---|---|
| Healthy volunteers | ○ Yes ◉ No ○ Not Answered |
| Patients | ◉ Yes ○ No ○ Not Answered |
| Specific vulnerable populations | ◉ Yes ○ No ○ Not Answered |
| Women of childbearing potential not using contraception | ○ Yes ◉ No ○ Not Answered |
| Women of child bearing potential using contraception | ◉ Yes ○ No ○ Not Answered |
| Pregnant women | ○ Yes ◉ No ○ Not Answered |
| Nursing women | ○ Yes ◉ No ○ Not Answered |
| Emergency situations | ○ Yes ◉ No ○ Not Answered |
| Subjects incapable of giving consent personally | ○ Yes ◉ No ○ Not Answered |
| Others | ○ Yes ◉ No ○ Not Answered |

**F4. Planned number of subjects to be included:**

In the member state 10

For a multinational trial:

In the European community: 16

In the whole clinical trial: 120

**F5. Plans for treatment or care after a subject has ended his/her participation in the trial.** ***If it is different from the expected normal treatment, please specify:***

Once a subject has completed study participation, the long-term care of the subject will be the responsibility of their primary treating physicians.

## G1. and G2. Investigator Details

**G1. National coordinating investigator** (for a multicentre trial) **or principal investigator** (for a single centre trial)

- ○ National coordinating investigator
- ◉ Principal investigator

| | |
|---|---|
| Given name | PPD |
| Family name | PPD |
| Qualification (MD...) | PPD |
| Institution name | King's College Hospital NHS Foundation Trust |
| Institution department name | King's College Hospital |
| Street address | Denmark Hill |
| Town/city | London |
| Post Code | SE5 9RS |
| Country | United Kingdom |
| Telephone | PPD |
| Fax | PPD |
| E-mail | PPD |

**G2. Other principal Investigators** *(for a multicentre trial)*

**IN1**

| | |
|---|---|
| Given name | PPD |
| Family name | PPD |
| Qualification (MD...) | PPD |
| Institution name | North Manchester General Hospital |
| Institution department name | Department of Infectious Diseases |
| Street address | Delaunays Road, Crumpsall |
| Town/city | Manchester |
| Post Code | M8 5RB |
| Country | United Kingdom |
| Telephone | PPD |
| Fax | |
| E-mail | PPD |

*For multi-centre trials where the CI is also a local PI, please list the CI as a PI at G2 (single-centre).*

## G3. Central Technical Facility Details

**G3. 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.*

**Organisation**

| | |
|---|---|
| Central technical facility organisation name | Labcorp Central Laboratory Services SÀRL |

| | |
|---|---|
| Central technical facility organisation department | |
| Contact person Given name | |
| Contact person Family name | |
| Street address | Rue Moïse-Marcinhes 7 |
| Town/city | Meyrin/Genève |
| Post code | CH - 1217 |
| Country | Switzerland |
| Work Telephone | 0041 58 822 7901 |
| Fax | 0041 58 822 7521 |
| E-mail | |

**Enter the details of any duties subcontracted to this central technical facility in this trial:**

| | |
|---|---|
| Routine clinical pathology testing | (●) Yes ( ) No ( ) Not Answered |
| Clinical chemistry | (●) Yes ( ) No ( ) Not Answered |
| Clinical haematology | (●) Yes ( ) No ( ) Not Answered |
| Clinical microbiology | (●) Yes ( ) No ( ) Not Answered |
| Histopathology | ( ) Yes (●) No ( ) Not Answered |
| Serology / endocrinology | (●) Yes ( ) No ( ) Not Answered |
| Analytical chemistry | ( ) Yes (●) No ( ) Not Answered |
| ECG analysis / review | ( ) Yes (●) No ( ) Not Answered |
| Medical image analysis/ review - X-ray, MRI, ultrasound, etc. | ( ) Yes (●) No ( ) Not Answered |
| Primary/ surrogate endpoint test | ( ) Yes (●) No ( ) Not Answered |
| Other | (●) Yes ( ) No ( ) Not Answered |

If "Other", specify the other duties

Pharmacokinetics, Pharmacogenomics, Biomarker analysis

**Organisation**

| | |
|---|---|
| Central technical facility organisation name | Labcorp Development (Asia) Pte. Limited |
| Central technical facility organisation department | |
| Contact person Given name | |
| Contact person Family name | |
| Street address | 1, International Business Park #01-01 The Synergy |
| Town/city | Singapore |
| Post code | 609917 |
| Country | Singapore |
| Work Telephone | 65 6560-8793 |
| Fax | 65 6565-5901 |
| E-mail | |

**Enter the details of any duties subcontracted to this central technical facility in this trial:**

| | |
|---|---|
| Routine clinical pathology testing | (•) Yes ( ) No ( ) Not Answered |
| Clinical chemistry | (•) Yes ( ) No ( ) Not Answered |
| Clinical haematology | (•) Yes ( ) No ( ) Not Answered |
| Clinical microbiology | (•) Yes ( ) No ( ) Not Answered |
| Histopathology | ( ) Yes (•) No ( ) Not Answered |
| Serology / endocrinology | (•) Yes ( ) No ( ) Not Answered |
| Analytical chemistry | ( ) Yes (•) No ( ) Not Answered |
| ECG analysis / review | ( ) Yes (•) No ( ) Not Answered |
| Medical image analysis/ review - X-ray, MRI, ultrasound, etc. | ( ) Yes (•) No ( ) Not Answered |
| Primary/ surrogate endpoint test | ( ) Yes (•) No ( ) Not Answered |
| Other | ( ) Yes (•) No ( ) Not Answered |

**Organisation**

| | |
|---|---|
| Central technical facility organisation name | Labcorp Central Laboratory Services LP |
| Central technical facility organisation department | |
| Contact person Given name | |
| Contact person Family name | |
| Street address | 8211 SciCor Drive |
| Town/city | Indianapolis, IN |
| Post code | 46214-2985 |
| Country | United States |
| Work Telephone | 00 317 271-1200 |
| Fax | 00 317 616-2362 |
| E-mail | |

**Enter the details of any duties subcontracted to this central technical facility in this trial:**

| | |
|---|---|
| Routine clinical pathology testing | (•) Yes ( ) No ( ) Not Answered |
| Clinical chemistry | (•) Yes ( ) No ( ) Not Answered |
| Clinical haematology | (•) Yes ( ) No ( ) Not Answered |
| Clinical microbiology | (•) Yes ( ) No ( ) Not Answered |
| Histopathology | ( ) Yes (•) No ( ) Not Answered |
| Serology / endocrinology | (•) Yes ( ) No ( ) Not Answered |
| Analytical chemistry | ( ) Yes (•) No ( ) Not Answered |

| | |
|---|---|
| ECG analysis / review | ○ Yes ◉ No ○ Not Answered |
| Medical image analysis/ review - X-ray, MRI, ultrasound, etc. | ○ Yes ◉ No ○ Not Answered |
| Primary/ surrogate endpoint test | ○ Yes ◉ No ○ Not Answered |
| Other | ◉ Yes ○ No ○ Not Answered |

If "Other", specify the other duties

Pharmacokinetics, Pharmacogenomics, Biomarker analysis

## Network organisation details

**G4. Network organisation details**

Organisation
Contact person Given name
Contact person Middle name
Contact person Family name
Street address
Town/city
PostCode
Country
Telephone number
Fax number
E-mail

Activities carried out by the network

## G5. Organisations to whom the sponsor has transferred trial related duties and functions

**G5. Subcontractor organisations.**
*Enter details of central CRO facilities supplying services for at least this Member State.*

| | |
|---|---|
| Organisation | Pharmaceutical Research Associates, Inc. |
| Department | |
| Contact person Given name | PPD |
| Contact person Family name | PPD |
| Street address | 4130 Parklake Avenue, Suite 400 |
| Town/city | Raleigh |
| PostCode | NC27612 |
| Country | United States |
| Telephone number | |
| Fax | |
| E-mail | PPD |

**Enter the details of any duties/ functions subcontracted to this sponsor's subcontractor facility in this trial**

All tasks of the sponsor: ○ Yes ◉ No ○ Not Answered

| | |
|---|---|
| Monitoring: | (•) Yes ( ) No ( ) Not Answered |
| Regulatory (e.g. preparation of applications to CA and Ethics Committee): | (•) Yes ( ) No ( ) Not Answered |
| Investigator recruitment: | (•) Yes ( ) No ( ) Not Answered |
| IVRS(1) - treatment randomisation: | ( ) Yes (•) No ( ) Not Answered |
| Data management: | ( ) Yes (•) No ( ) Not Answered |
| E-data capture: | (•) Yes ( ) No ( ) Not Answered |
| SUSAR reporting: | ( ) Yes (•) No ( ) Not Answered |
| Quality assurance auditing: | ( ) Yes (•) No ( ) Not Answered |
| Statistical analysis: | ( ) Yes (•) No ( ) Not Answered |
| Medical writing: | ( ) Yes (•) No ( ) Not Answered |
| Other duties subcontracted: | (•) Yes ( ) No ( ) Not Answered |

If yes to others, please specify:

medical monitoring, screening, enrolment, IP management, eCRF

## H: Ethics Committee

**H1-1. Type of application**
*Please tick the Ethics Committee box and give information of the Ethics committee concerned.*

Ethics committee ☑

**H2-1. Limited Name and address of ethics committee:**

Organisation Pending
Work Address

PostCode
Country
Fax

**H2-2. Date of submission:**

**H2-3. Current status of Ethics Committee Opinion at the time of submission to the National Competent Authority:**

◉ To be requested ○ Pending ○ Given

## I: Signature Of The Applicant In The Member State

**I1. I hereby confirm that /confirm on behalf of the sponsor (tick which is 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;

☑ The clinical trial will be conducted, and SUSARs and result-related information will be reported, in accordance with the applicable legislation.

**I2. Applicant of the request for the competent authority** (as stated in section C.1):

Date .....10-September-2021.....

Signature .....PPD.....

Print name ....PPD.....

## J: Checklist

**J3.** ***For details of the documents required for applications to the MHRA in the UK please see*** ***http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Applyingforaclinicaltrialauthorisation/Whattosend/index.htm***