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:	**UK - MHRA**
A.2	EudraCT number:	**2019-004475-39**
A.3	Full title of the trial:	
	English	**A Phase 2 Randomized, Open-label, Parallel-group, Multicenter Study to Assess Intrahepatic and Peripheral Changes of Immunologic and Virologic Markers in Response to Combination Regimens Containing JNJ-73763989 and Nucleos(t)ide Analog With or Without JNJ-56136379 in Patients With Chronic Hepatitis B Virus Infection.**
A.3.1	Title of the trial for lay people, in easily understood, i.e. non-technical, language:	
	English	**A Clinical Study to Assess Immunologic and Virologic Changes in the Liver in Response to Combination Regimens Containing JNJ-73763989 and Nucleos(t)ide Analog With or Without JNJ-56136379 in Patients With Chronic Hepatitis B Virus Infection.**
A.3.2	Name or abbreviated title of the trial where available:	
	English	**INSIGHT**
A.4	Sponsor's protocol code number, version and date[1]:	
A.4.1	Sponsor's protocol code number:	**73763989HPB2003**
A.4.2	Sponsor's protocol version:	**Amendment2**
A.4.3	Sponsor's protocol date:	**2020-05-07**
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:	
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:	**Janssen Sciences Ireland Unlimited Company**
B.1.2	Name of the person to contact:	
B.1.2.1	Given name	[redacted]
B.1.2.2	[redacted]	[redacted]

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:
B.2.2	Name of person to contact:
B.2.2.1	Given name
B.2.2.2	Middle name
B.2.2.3	Family name
B.2.3	Address:
B.2.3.1	Street address
B.2.3.2	Town/city
B.2.3.3	Post code
B.2.3.4	Country
B.2.4	Telephone number:
B.2.5	Fax number:
B.2.6	E-mail:

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

B.4	**Source(s) of Monetary or Material Support for the clinical trial (repeat as necessary):**	
B.4.1	Name of organisation:	**Janssen Sciences Ireland Unlimited Company**
B.4.2	Country:	**Ireland**

B.5	**Contact point[6] designated by the sponsor for further information on the trial**	
B.5.1	Name of organisation:	**Janssen-Cilag International NV**
B.5.2	Functional name of contact point (e.g. "Clinical Trial Information Desk"):	**Clnical Registry Group**
B.5.3	Address:	
B.5.3.1	Street address	**Archimedesweg 29**
B.5.3.2	Town/city	**Leiden**
B.5.3.3	Post code	**2333 CM**
B.5.3.4	Country	**Netherlands**
B.5.4	Telephone number:	
B.5.5	Fax number:	
B.5.6	E-mail: (use a functional e-mail address rather than a personal one)	**clinicaltrialsEU@its.jnj.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:	**Janssen-Cilag Ltd**
C.1.4.2	Name of contact person:	
C.1.4.2.1	Given name	[redacted]
C.1.4.2.2	Middle name	
C.1.4.2.3	Family name	
C.1.4.3	Address:	
C.1.4.3.1	Street address	[redacted]
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?	**Not Answered •**

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** **Czech Republic** **France** **Germany** **Italy** **Poland** **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?	**No •**
D.2.6.1	If 'Yes' to D.2.6, please indicate source of advice and provide a copy in the CTA request:	
D.2.6.1.1	CHMP[11]?	**No •**
D.2.6.1.2	National Competent Authority?	**No •**

D.3	**DESCRIPTION OF THE IMP**	
D.3.1	Product name where applicable[12]:	
D.3.2	Product code where applicable[13]:	**JNJ-73763989**
D.3.3	ATC codes, if officially registered[14]:	
D.3.4	Pharmaceutical form (use standard terms):	**Solution for injection**
D.3.4.1	Is this a specific paediatric formulation?	**No •**
D.3.5	Maximum duration of treatment of a subject according to the protocol:	
	48 weeks	
D.3.6	Dose allowed:	
D.3.6.1	For first trial only:	
	Specify per day or total	**Total •**
	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):	[redacted] **mg milligram(s)**
	Route of administration (relevant to the maximum dose):	**Subcutaneous use**
D.3.7	Routes of administration (use standard terms):	**Subcutaneous use**

D.3.8	Name of each active substance (INN or proposed INN if available):	
	Not yet assigned	
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	**JNJ-73763989-AAM**
D.3.9.3	Other descriptive name	
	JNJ-73763989-AAM	
D.3.9.4	EV Substance code	**SUB197801**
D.3.9.5	Full Molecular formula	
D.3.9.6	Chemical/biological description of the Active Substance	
	Please see IB and qIMPD.	
D.3.10	Strength (specify all strengths to be used):	
D.3.10.1	Concentration unit:	**mg/ml milligram(s)/millilitre**
D.3.10.2	Concentration type ("exact number", "range", "more than" or "up to"):	**equal**
D.3.10.3	Concentration (number).	[redacted]

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]) **JNJ-73763989 injection is a liver-targeted antiviral therapeutic designed to treat chronic HBV infection via an RNAi mechanism.**	
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?	**Not Answered •**

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** **Czech Republic** **France** **Germany** **Italy** **Poland** **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?	**No •**
D.2.6.1	If 'Yes' to D.2.6, please indicate source of advice and provide a copy in the CTA request:	
D.2.6.1.1	CHMP[11]?	**No •**
D.2.6.1.2	National Competent Authority?	**No •**

D.3	**DESCRIPTION OF THE IMP**	
D.3.1	Product name where applicable[12]:	
D.3.2	Product code where applicable[13]:	**JNJ-56136379**
D.3.3	ATC codes, if officially registered[14]:	
D.3.4	Pharmaceutical form (use standard terms):	**Tablet**
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: **48 weeks**	
D.3.6	Dose allowed:	
D.3.6.1	For first trial only:	
	Specify per day or total	**Total •**
	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):	[redacted] **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 yet assigned**	
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	**JNJ-56136379**
D.3.9.3	Other descriptive name **JNJ-56136379-AAA**	
D.3.9.4	EV Substance code	**SUB180015**
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).	[redacted]

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	**No •**

	device[19])?	
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]) **JNJ-56136379 binds to the HBV core protein and interferes with the viral capsid assembly process, thereby preventing the Pol-pgRNA encapsidation. This results in the formation of HBV capsids, devoid of HBV DNA, and ultimately in the inhibition of HBV replication in vitro. In addition, JNJ-56136379 also acts at an early stage of the viral life cycle by inhibiting the de novo formation of covalently closed circular DNA potentially by interfering with the capsid disassembly process.**	
D.3.13	Is it an IMP to be used in a first-in-human clinical trial?	**No** •
D.3.13.1	If 'Yes', are there risk factors identified, according to the guidance FIH?[21]	

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

D.5	**GENE THERAPY INVESTIGATIONAL MEDICINAL PRODUCTS**	
D.5.1	Gene(s) of interest:	
D.5.2	In vivo gene therapy:	**No** •
D.5.3	Ex vivo gene therapy:	**No** •
D.5.4	Type of gene transfer product	
D.5.4.1	Nucleic acid (e.g. plasmid): If 'Yes', specify if:	**No** •
D.5.4.1.1	Naked:	**No** •
D.5.4.1.2	Complexed	**No** •
D.5.4.2	Viral vector:	**No** •

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

D.6 TISSUE ENGINEERED PRODUCT

The indication which determines that this is a Tissue Engineered Product as opposed to a Cell Therapy product is given in section E.1.1.

D.6.1	Origin of cells	
D.6.1.1	Autologous	**No •**
D.6.1.2	Allogeneic	**No •**
D.6.1.3	Xenogeneic	**No •**
D.6.1.3.1	If 'Yes', specify the species of origin:	
D.6.2	Type of cells	
D.6.2.1	Stem cells	**No •**
D.6.2.2	Differentiated cells	**No •**
D.6.2.2.1	If 'Yes', specify the type of cells(e.g. keratinocytes, fibroblasts, chondrocytes, …):	
D.6.2.3	Others:	**No •**
D.6.2.3.1	If others, specify:	

D.7 PRODUCTS CONTAINING DEVICES (i.e. MEDICAL DEVICES, SCAFFOLDS ETC.)

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

D.1 IMP IDENTIFICATION

Indicate which of the following is described below, then repeat as necessary for each of the numbered IMPs to be used in the trial (assign numbers from 1-n):

D.1.1	This refers to the IMP number:	**PR3**
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?	**Not Answered •**

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** **Czech Republic** **France** **Germany** **Italy** **Poland** **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?	**No •**
D.2.6.1	If 'Yes' to D.2.6, please indicate source of advice and provide a copy in the CTA request:	
D.2.6.1.1	CHMP[11]?	**No •**
D.2.6.1.2	National Competent Authority?	**No •**

D.3	DESCRIPTION OF THE IMP	
D.3.1	Product name where applicable[12]:	
D.3.2	Product code where applicable[13]:	**JNJ-56136379**
D.3.3	ATC codes, if officially registered[14]:	
D.3.4	Pharmaceutical form (use standard terms):	**Tablet**
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: **48 weeks**	
D.3.6	Dose allowed:	
D.3.6.1	For first trial only:	
	Specify per day or total	**Total •**
	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):	[redacted] **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 yet assigned**	
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	**JNJ-56136379**
D.3.9.3	Other descriptive name **JNJ-56136379-AAA**	
D.3.9.4	EV Substance code	**SUB180015**
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).	[redacted]

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]) **JNJ-56136379 binds to the HBV core protein and interferes with the viral capsid assembly process, thereby preventing the Pol-pgRNA encapsidation. This results in the formation of HBV capsids, devoid of HBV DNA, and ultimately in the inhibition of HBV replication in vitro. In addition, JNJ-56136379 also acts at an early stage of the viral life cycle by inhibiting the de novo formation of covalently closed circular DNA potentially by interfering with the capsid disassembly process.**	
D.3.13	Is it an IMP to be used in a first-in-human clinical trial?	**No •**
D.3.13.1	If 'Yes', are there risk factors identified, according to the guidance FIH?[21]	

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

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

D.5.5.2	Allogeneic:	**No •**
D.5.5.3	Xenogeneic:	**No •**
D.5.5.3.1	If 'Yes', specify the species of origin:	
D.5.5.4	Specify type of cells (hematopoietic stem cells…):	

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

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

D.1	**IMP IDENTIFICATION**	
Indicate which of the following is described below, then repeat as necessary for each of the numbered IMPs to be used in the trial (assign numbers from 1-n):		
D.1.1	This refers to the IMP number:	**PR4**
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?	**Yes •**
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	**Entecavir Mylan 0.5 mg film-coated tablets**
D.2.1.1.1.1	EV Product Code (where applicable)	
D.2.1.1.2	Name of the Marketing Authorisation Holder:	**Mylan S.A.S.**

D.2.1.1.3	Marketing Authorisation number (if Marketing Authorisation granted by a Member State):	**EU/1/17/1227/001 - 010**
D.2.1.1.4	Is the IMP modified in relation to its Marketing Authorisation?	**No •**
D.2.1.1.4.1	If 'Yes', please specify:	
D.2.1.2	The country that granted the Marketing Authorisation	**European Union**
D.2.1.2.1	Is this the Member State concerned with this application?	**Not Answered •**

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?	**Yes •**
D.2.2.1.1	If 'Yes', give active substance in D.3.8 or D.3.9	
D.2.2.2	In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?	**No •**
D.2.2.2.1	If 'Yes', give active substance in D.3.8 or D.3.9	
D.2.2.3	The products to be administered as IMPs are defined as belonging to an ATC group[9]	**No •**
D.2.2.3.1	If 'Yes', give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.3	
D.2.2.4	Other:	**No •**
D.2.2.4.1	If 'Yes', please specify:	

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

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

D.3	**DESCRIPTION OF THE IMP**	
D.3.1	Product name where applicable[12]:	
D.3.2	Product code where applicable[13]:	
D.3.3	ATC codes, if officially registered[14]:	**J05AF10**
D.3.4	Pharmaceutical form (use standard terms):	**Film-coated tablet**
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 weeks**	
D.3.6	Dose allowed:	
D.3.6.1	For first trial only:	
	Specify per day or total	**Total •**
	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):	**0.5 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):	
	Entecavir	
D.3.9	Other available name for each active substance (provide all available):	
D.3.9.1	CAS[15] number	
D.3.9.2	Current sponsor code	
D.3.9.3	Other descriptive name	
	ENTECAVIR MONOHYDRATE	
D.3.9.4	EV Substance code	**SUB25434**
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).	**0.5**

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])	

	Entecavir, a guanosine nucleoside analogue with activity against HBV polymerase, is phosphorylated to the active triphosphate (TP) form, which has an intracellular halflife of 15 hours. By competing with the natural substrate deoxyguanosine TP, entecavir-TP functionally inhibits the 3 activities of the viral polymerase: (1) priming of the HBV polymerase, (2) reverse transcription of the negative strand DNA from the pregenomic messenger RNA, and (3) synthesis of the positive strand HBV DNA.	
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:	**PR5**
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?	**Yes •**
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 **Vemlidy 25 mg film-coated tablets**	
D.2.1.1.1.1	EV Product Code (where applicable)	
D.2.1.1.2	Name of the Marketing Authorisation Holder:	**Gilead Sciences Ireland UC**
D.2.1.1.3	Marketing Authorisation number (if Marketing Authorisation granted by a Member State):	**EU/1/16/1154/001 - 002**
D.2.1.1.4	Is the IMP modified in relation to its Marketing Authorisation?	**No •**
D.2.1.1.4.1	If 'Yes', please specify:	
D.2.1.2	The country that granted the Marketing Authorisation	**European Union**
D.2.1.2.1	Is this the Member State concerned with this application?	**Not Answered •**

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?	**Yes •**
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	**No •**

	combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?	
D.2.2.2.1	If 'Yes', give active substance in D.3.8 or D.3.9	
D.2.2.3	The products to be administered as IMPs are defined as belonging to an ATC group[9]	**No •**
D.2.2.3.1	If 'Yes', give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.3	
D.2.2.4	Other:	**No •**
D.2.2.4.1	If 'Yes', please specify:	

D.2.3	IMPD submitted:	
D.2.3.1	Full IMPD:	**No •**
D.2.3.2	Simplified IMPD:	**Yes •**
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** **Czech Republic** **France** **Germany** **Italy** **Poland** **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?	**No •**
D.2.6.1	If 'Yes' to D.2.6, please indicate source of advice and provide a copy in the CTA request:	
D.2.6.1.1	CHMP[11]?	**No •**
D.2.6.1.2	National Competent Authority?	**No •**

D.3	**DESCRIPTION OF THE IMP**	
D.3.1	Product name where applicable[12]:	
D.3.2	Product code where applicable[13]:	
D.3.3	ATC codes, if officially registered[14]:	**J05AF13**
D.3.4	Pharmaceutical form (use standard terms):	**Film-coated tablet**
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 weeks	
D.3.6	Dose allowed:	
D.3.6.1	For first trial only:	
	Specify per day or total	**Total •**
	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):	**25 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):

	TENOFOVIR ALAFENAMIDE	
D.3.9	Other available name for each active substance (provide all available):	
D.3.9.1	CAS[15] number	**379270-37-8**
D.3.9.2	Current sponsor code	
D.3.9.3	Other descriptive name	
D.3.9.4	EV Substance code	**SUB121761**
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).	**25**

D.3.11	Type of IMP	
Does the IMP contain an active substance:		
D.3.11.1	Of chemical origin?	**Yes •**
D.3.11.2	Of biological / biotechnological origin (other than Advanced Therapy IMP (ATIMP)?	**No •**
Is this a:		
D.3.11.3	Advanced Therapy IMP (ATIMP)?	**No •**
D.3.11.3.1	Somatic cell therapy medicinal product[16]?	**No •**
D.3.11.3.2	Gene therapy medicinal product[17]?	**No •**
D.3.11.3.3	Tissue Engineered Product[18]?	**No •**
D.3.11.3.4	Combination ATIMP (i.e. one involving a medical device[19])?	**No •**
D.3.11.3.5	Has the Committee on Advanced Therapies issued a classification for this product?	**No •**
D.3.11.3.5.1	If 'Yes' please provide that classification and its reference number:	
D.3.11.4	Combination product that includes a device, but does not involve an Advanced Therapy?	**No •**
D.3.11.5	Radiopharmaceutical medicinal product?	**No •**
D.3.11.6	Immunological medicinal product (such as vaccine, allergen, immune serum)?	**No •**
D.3.11.7	Plasma derived medicinal product?	**No •**
D.3.11.8	Extractive medicinal product?	**No •**
D.3.11.9	Recombinant medicinal product?	**No •**
D.3.11.10	Medicinal product containing genetically modified organisms?	**No •**
D.3.11.10.1	Has the authorisation for contained use or release been granted?	**No •**
D.3.11.10.2	Is it pending?	**No •**
D.3.11.11	Herbal medicinal product?	**No •**
D.3.11.12	Homeopathic medicinal product?	**No •**
D.3.11.13	Another type of medicinal product?	**No •**
D.3.11.13.1	If 'another type of medicinal product' specify the type of medicinal product:	
D.3.12	Mode of action (*free text*[20])	
	Tenofovir alafenamide is primarily hydrolyzed to form tenofovir by carboxylesterase 1 in primary hepatocytes. Intracellular tenofovir is subsequently phosphorylated to the pharmacologically active metabolite tenofovir diphosphate. Tenofovir diphosphate inhibits HBV replication through incorporation into viral DNA by the HBV reverse transcriptase, which results in DNA chain termination.	
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:	**PR6**
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?	**Yes •**
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	**Tenofovir disoproxil Mylan 245 mg film-coated tablets**
D.2.1.1.1.1	EV Product Code (where applicable)	
D.2.1.1.2	Name of the Marketing Authorisation Holder:	**MYLAN S.A.S**
D.2.1.1.3	Marketing Authorisation number (if Marketing Authorisation granted by a Member State):	**EU/1/16/1129/001 - 005**
D.2.1.1.4	Is the IMP modified in relation to its Marketing Authorisation?	**No •**
D.2.1.1.4.1	If 'Yes', please specify:	
D.2.1.2	The country that granted the Marketing Authorisation	**European Union**
D.2.1.2.1	Is this the Member State concerned with this application?	**Not Answered •**

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?	**Yes •**
D.2.2.1.1	If 'Yes', give active substance in D.3.8 or D.3.9	
D.2.2.2	In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?	**No •**
D.2.2.2.1	If 'Yes', give active substance in D.3.8 or D.3.9	
D.2.2.3	The products to be administered as IMPs are defined as belonging to an ATC group[9]	**No •**
D.2.2.3.1	If 'Yes', give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.3	

D.2.2.4	Other:	**No •**
D.2.2.4.1	If 'Yes', please specify:	

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

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

D.3	**DESCRIPTION OF THE IMP**	
D.3.1	Product name where applicable[12]:	
D.3.2	Product code where applicable[13]:	
D.3.3	ATC codes, if officially registered[14]:	**J05AF07**
D.3.4	Pharmaceutical form (use standard terms):	**Film-coated tablet**
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 weeks**	
D.3.6	Dose allowed:	
D.3.6.1	For first trial only:	
	Specify per day or total	**Total •**
	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):	**245 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): **TENOFOVIR DISOPROXIL**	
D.3.9	Other available name for each active substance (provide all available):	
D.3.9.1	CAS[15] number	
D.3.9.2	Current sponsor code	
D.3.9.3	Other descriptive name **TENOFOVIR DISOPROXIL**	
D.3.9.4	EV Substance code	**SUB20643**
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).	**245**

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])	
	Tenofovir disoproxil is absorbed and converted to the active substance tenofovir. Tenofovir is converted to the active metabolite, tenofovir diphosphate. Tenofovir diphosphate inhibits HIV-1 reverse transcriptase and the HBV polymerase by direct binding competition with the natural deoxyribonucleotide substrate and, after incorporation into DNA, by DNA chain termination.	
D.3.13	Is it an IMP to be used in a first-in-human clinical trial?	**No •**
D.3.13.1	If 'Yes', are there risk factors identified, according to the guidance FIH?[21]	

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

D.4.2.3.1	If others, specify:	

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

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

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

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

D.8.1	Is there a placebo:	**No •**

D.8.2	This refers to placebo number:	
D.8.3	Pharmaceutical form:	
D.8.4	Route of administration:	
D.8.5	Which IMP is it a placebo for? Specify IMP Number(s) from D.1.1	
D.8.5.1	Composition, apart from the active substance(s):	
D.8.5.2	Is it otherwise identical to the IMP?	**Yes ? No ? Not Answered ?**
D.8.5.2.1	If not, specify major ingredients:	

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

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

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

D.9.2	Who is responsible in the Community for the certification of the finished IMPs?	
	This site is responsible for certification of (list the number(s) of each IMP including placebo from sections D.1.1 and D.8.2):	**PR1** **PR2** **PR3** **PR4** **PR5** **PR6**

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:	[redacted]
D.9.2.4	Address:	
D.9.2.4.1	Street Address	[redacted]
D.9.2.4.2	Town/City	[redacted]
D.9.2.4.3	Post Code	[redacted]
D.9.2.4.4	Country	[redacted]
D.9.2.5	Give the manufacturing authorisation number:	**2 IMP**
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	**Chronic Hepatitis B Virus Infection**			
E.1.1.1	Medical condition in easily understood language				
	English	**Chronic Hepatitis B Virus Infection**			
E.1.1.2	Therapeutic area				
	Diseases [C] - Virus Diseases [C02]				
E.1.2	MedDRA version, system organ class, level, term and classification code[24]:				
	Version	System Organ Class	Classification Code	Term	Level
	20.1	**10021881 - Infections and infestations**	**10008910**	**Chronic hepatitis B**	**PT**
E.1.3	Is any of the conditions being studied a rare disease[25]?			**No •**	

E.2	OBJECTIVE OF THE TRIAL	
E.2.1	Main objective:	
	English	**To assess changes in intrahepatic HBsAg between baseline and on-treatment liver biopsy in response to JNJ-3989-based combination treatment**
E.2.2	Secondary objectives:	
	English	**1. To assess changes in intrahepatic immune response between baseline and on-treatment liver biopsy.** **2. To assess changes in intrahepatic viral nucleic acids and proteins between baseline and on-treatment liver biopsy.** **3. To evaluate the efficacy of the study intervention as measured in the periphery.** **4. To evaluate the frequency of virologic breakthrough during study intervention.** **5. To assess HBV-specific T-cell responses.** **6. To evaluate the safety and tolerability of the study intervention.** **7. To evaluate the plasma PK of JNJ-3989 (ie, JNJ-3976 and JNJ-3924), JNJ-6379, and optionally of NA, as applicable.**
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	**1. Adult participants ≥18 years of age (or the legal age of consent in the jurisdiction in which the study is taking place) to ≤65 years of age.** **2. Participants must be medically stable on the basis of physical examination, medical history, vital signs, and triplicate 12-lead ECG performed at screening. Any abnormalities must be consistent with the underlying illness in the study population and this determination must be recorded in the participant's source documents and initialed by the investigator.** **3. Participants must have HBV infection documented by serum HBsAg positivity at screening. In addition, chronicity must be documented by any of the following at least 6 months prior to screening: serum HBsAg positivity, HBeAg positivity or HBV DNA positivity, ALT elevation above**

ULN without another cause than HBV infection, documented transmission event, liver biopsy with changes consistent with chronic HBV. If none of the above are available, the following ways of documenting chronicity are acceptable at the time of screening: absence of marker for acute infection such as immunoglobulin M (IgM) anti-HBs and anti-HBc antibodies, which can be tested at screening.
4. Participants who are not currently treated (defined as not having been on HBV treatment, including NAs and IFN products within 6 months prior to screening), including treatment-naïve participants (defined as never having received HBV treatment, including NAs and IFN products) should:
a. be HBeAg positive, AND
b. have serum HBV DNA at screening ≥20,000 IU /mL, AND
c. have ALT levels at screening <10x ULN, AND
d. have indication for NA treatment according to local standard practice.
5. Virologically suppressed participants should:
a. be HBeAg negative, AND
b. be on stable HBV treatment, defined as currently receiving NA treatment (ETV, tenofovir disoproxil, or TAF) for at least 6 months prior to screening and have been on the same NA treatment regimen (at the same dose) for at least 3 months at the time of screening, AND
c. have serum HBV DNA <60 IU/mL on 2 measurements at least 3 months apart (one of which is at screening), AND
d. have documented ALT values <2.0x ULN on 2 measurements at least 3 months apart (one of which is at screening).
6. Participants must have HBsAg >100 IU/mL at screening.
7. Participants must have a body mass index (weight in kg divided by the square of height in meters) between 18.0 and 35.0 kg/m2, extremes included.
8. Participants must have fibroscan liver stiffness measurement ≤9.0 kPa within 6 months prior to screening or at the time of screening.
9.Female participants of childbearing potential must have a negative highly sensitive serum pregnancy test (B-human chorionic gonadotropin [B-hCG]) at screening and a negative urine pregnancy test on Day 1 before the first dose of study intervention.
10. A woman must be (as defined in Section 10.8, Appendix 8, Contraceptive and Barrier Guidance and Collection of Pregnancy Information):
a. not of childbearing potential
b. of childbearing potential and practicing a highly effective, preferably user-independent method of contraception (failure rate of <1% per year when used consistently and correctly) for at least 30 days prior to screening and agrees to remain on a highly effective method while receiving study intervention and until 90 days after last dose of study intervention.
Examples of highly effective methods of contraception are located in Section 10.8, Appendix 8, Contraceptive and Barrier Guidance and Collection of Pregnancy Information.
11. Male participants must agree to wear a condom when engaging in any activity that allows for passage of ejaculate to another person during the study intervention period and until 90 days after last dose of study intervention.
12. Female participants must agree not to donate eggs (ova, oocytes) for the purposes of assisted reproduction during the study intervention period and until 90 days after last dose of study intervention.
13. Male participants must agree not to donate sperm for the purpose of reproduction during the study intervention phase and until 90 days after last dose of study intervention.
14. Participants must sign an ICF indicating that he or she understands the purpose of, and procedures required for, the study and is willing to participate in the study.
15. Participants must separately consent if he or she agrees to undergo

	optional study procedures (ie, leukapheresis, intensive PK, and/or optional biopsy). Refusal to give consent to one or all of these optional study procedures does not exclude from participation in the study. **16. In the investigator's opinion, the participant is able to understand and comply with protocol requirements, instructions, and study restrictions and is likely to complete the procedures as planned for this this study.** **Please refer to the protocol for a full list of the inclusion criteria.**

E.4	**PRINCIPAL EXCLUSION CRITERIA *(list the most important)***
	English	**1. Participants with evidence of hepatitis A virus infection (hepatitis A antibody IgM), HCV infection (HCV antibody), hepatitis D virus (HDV) infection (HDV antibody), or hepatitis E virus (HEV) infection (HEV antibody IgM), or HIV-1 or HIV-2 infection (confirmed by antibodies) at screening.** **2. Participants with any of the following laboratory abnormalities within 12 months prior to screening or at the time of screening:** **a. Total bilirubin >1.5x ULN, OR** **b. Direct bilirubin >1.2x ULN, OR** **c. Serum albumin <3.2 g/dL,** **3. History or evidence of clinical signs/symptoms of hepatic decompensation including but not limited to: portal hypertension, ascites, hepatic encephalopathy, esophageal varices.** **4. Participants with evidence of liver disease of non-HBV etiology. This includes but is not limited to hepatitis virus infections mentioned in exclusion criterion 1, drug- or alcohol related liver disease, autoimmune hepatitis, hemochromatosis, Wilson's disease, α 1 antitrypsin deficiency, primary biliary cholangitis, primary sclerosing cholangitis, Gilbert's syndrome (mild cases are allowed, see exclusion criterion 2a), or any other non HBV liver disease considered clinically significant by the investigator.** **5. Participants with history or signs of cirrhosis or portal hypertension (nodules, no smooth liver contour, no normal portal vein, spleen size ≥ 12 cm), signs of HCC or clinically relevant renal abnormalities on an abdominal ultrasound performed within 6 months prior to screening or at the time of screening.** **6. Participants with one or more of the following laboratory abnormalities at screening as defined by the Division of Acquired Immunodeficiency Syndrome (DAIDS) Toxicity Grading Scale:** **a. Estimated glomerular filtration rate (eGFR) ≥grade 3 (<60 mL/min/1.73m²), calculated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula;** **b. Pancreatic lipase elevation ≥grade 3;** **c. Pancreatic amylase elevation ≥grade 3** **d. Hemoglobin ≤10.9 g/dL (males), ≤10.4 g/dL (females);** **e. Platelet count ≤lower limit of normal (LLN);** **f. Alpha-fetoprotein (AFP) >100 ng/mL;** **g. Any other laboratory abnormality considered to be clinically significant by the investigator.** **7. Participants with presence of coagulopathy or bleeding disorder as indicated by:** **a. International normalized ratio (INR) ≥1.1 x ULN;** **b. Partial thromboplastin time > 1.1 x ULN;** **c. Any signs of prolonged bleeding (>10 minutes).** **8. Participants with presence of hemoglobinopathy (including sickle cell disease, thalassemia).** **9. Participants who had a liver biopsy performed prior to screening that led to complications and that in the opinion of the investigator would**

prohibit another liver biopsy.
10. Participants with history of amyloidosis.
11. Participant refusal to accept blood transfusions.
12. Participants with hemoglobin A1c >8% at screening.
13. Participants with a history of malignancy within 5 years prior to screening (exceptions are squamous and basal cell carcinomas of the skin and carcinoma in situ of the cervix, or malignancy, which are considered cured with minimal risk of recurrence).
14. Participants with abnormal sinus rhythm (heart rate <45 or >100 beats per minute [bpm]); QT interval corrected for heart rate according to Fridericia's formula (QTcF) >450 ms for males and >470 ms for females; QRS interval ≥120 ms; PR interval >220 ms ; abnormal conduction; or any other clinically significant abnormalities on a 12-lead ECG at screening.
15. Participants with a history of or current cardiac arrhythmias (eg, extrasystole, tachycardia at rest), history of risk factors for Torsade de Pointes syndrome (eg, hypokalemia, family history of long QT Syndrome) or history or other clinical evidence of significant or unstable cardiac disease (eg, angina, congestive heart failure, myocardial infarction, diastolic dysfunction, significant arrhythmia and/or coronary heart disease), moderate to severe valvular disease, or uncontrolled hypertension at screening.

Please refer to the protocol for a full list of the exclusion criteria.

E.5	**END POINT(S):**	
E.5.1	Primary End Point (repeat as necessary)[26]	
	English	**Changes in the proportion of HBsAg positive hepatocytes between baseline and on-treatment Week 40.**
E.5.1.1	Timepoint(s) of evaluation of this end point	
	English	**Week 40**
E.5.2	Secondary End Point (repeat as necessary)	
	English	**1.Changes between baseline and on-treatment liver biopsy in intrahepatic immune response (eg, CD45+ T-cells, CD4+ T-cells, CD8+ T-cells,** **Natural Killer cells, and dendritic cells) in terms of proportion of cells, cell types, and spatial redistribution.** **2a. Changes from baseline in intrahepatic viral parameters (such as cccDNA, pgRNA, intrahepatic RNA, or HBsAg in terms of copy number, or number of positive cells).** **2b. Changes from baseline in intrahepatic cccDNA levels and transcriptional activity (pgRNA/cccDNA ratio).** **3a. The proportion of participants during the study intervention and follow-up phases with:** **-HBsAg seroclearance at Week 72 (ie, 24 weeks after completion of all study interventions at Week 48) without restarting NA treatment.** **-(Sustained) Reduction, suppression, and/or seroclearance considering single and multiple markers (such as HBsAg, HBeAg, HBV DNA and ALT)** **-HBsAg and HBeAg seroconversion** **-Flares (virologic, biochemical, and clinical)** **3b. Time to first HBsAg seroclearance** **4. Proportion of participants with virologic breakthrough.** **5. Changes from baseline in HBV-specific peripheral blood T-cell responses during the study intervention and follow-up phases.** **6. Proportion of participants with (S)AEs and abnormalities in clinical laboratory tests (including hematology, blood biochemistry, blood coagulation, urinalysis, urine chemistry, and renal biomarkers), 12-lead ECGs, vital signs, and physical examinations throughout the study.**

	7. Plasma PK parameters of JNJ-3976, JNJ-3924, JNJ-6379, and optionally of NA, as applicable.	
E.5.2.1	Timepoint(s) of evaluation of this end point **English**	**Throughout the study duration.**

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	**No •**
E.6.10	Pharmacogenetic	**No •**
E.6.11	Pharmacogenomic	**No •**
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 Is it:	Human pharmacology (Phase I)	**No •**
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)	**No •**
E.7.4	Therapeutic use(Phase IV)	**No •**

E.8	**DESIGN OF THE TRIAL**		
E.8.1	Controlled If 'Yes', specify:	**Yes •**	
E.8.1.1	Randomised:	**Yes •**	
E.8.1.2	Open:	**Yes •**	
E.8.1.3	Single blind:	**No •**	
E.8.1.4	Double blind:	**No •**	
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)	**Yes •**	
E.8.2.2	Placebo	**No •**	
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	**2**	
E.8.3	Single site in the Member State concerned (see also section G):		**Yes •**
E.8.4	Multiple sites in the Member State concerned(see also section G):		**No •**
E.8.4.1	Number of sites anticipated in Member State concerned		
E.8.5	Multiple Member States:	**Yes •**	
E.8.5.1	Number of sites anticipated in the EEA:	**7**	
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: **Belgium** **Canada** **France** **Germany** **Italy** **New Zealand** **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:	**3**
E.8.7	Trial having an independent data monitoring committee:	**No •**
E.8.8	Definition of the end of trial: If it is the last visit of the last subject, please enter "LVLS". If it is not LVLS provide the definition: **English** **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	**2 years 5 months 0 days**
E.8.9.2	In all countries concerned by the trial	**2 years 5 months 0 days**
E.8.10	Proposed date of start of recruitment	
E.8.10.1	In the Member State concerned	**2021-03-01**
E.8.10.2	In any country	**2020-05-19**

F. POPULATION OF TRIAL SUBJECTS

F.1	AGE RANGE		
F.1.1	Are the trial subjects under 18? If 'Yes', specify the estimated number of subjects planned in each age range for the whole trial:		**No •**
		Approx. No. of patients[29]	
F.1.1.1	In utero	()	**No •**
F.1.1.2	Preterm newborn infants (up to gestational age < 37 weeks)	()	**No •**
F.1.1.3	Newborns (0-27 days)	()	**No •**
F.1.1.4	Infants and toddlers (28 days - 23 months)	()	**No •**
F.1.1.5	Children (2-11 years)	()	**No •**
F.1.1.6	Adolescents (12-17 years)	()	**No •**
F.1.2	Adults (18-64 years)	(**24**)	**Yes •**
F.1.3	Elderly (>= 65 years)	()	**No •**

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	**Yes •**
F.3.3.3	Pregnant women	**No •**
F.3.3.4	Nursing women	**No •**
F.3.3.5	Emergency situation	**No •**
F.3.3.6	Subjects incapable of giving consent personally	**No •**
F.3.3.6.1	If 'Yes', specify:	
F.3.3.7	Others:	**No •**
F.3.3.7.1	If 'Yes', specify:	

F.4	PLANNED NUMBER OF SUBJECTS TO BE INCLUDED:	
F.4.1	In the member state	**3**
F.4.2	For a multinational trial**:**	
F.4.2.1	In the EEA	**14**
F.4.2.2	In the whole clinical trial	**24**

F.5 PLANS FOR TREATMENT OR CARE AFTER THE SUBJECT HAS ENDED HIS/HER PARTICIPATION IN THE TRIAL. please specify (free text):

English **Participants will be instructed that study intervention will not be made available to them after they have completed/discontinued study intervention and that they should return to their primary physician to determine standard of care.**

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

G.1	CO-ORDINATING INVESTIGATOR (for multicentre trial) and principal investigator (for single centre trial)	
G.1.1	Given name:	[redacted]
G.1.2	Middle name, if applicable:	
G.1.3	Family name:	[redacted]
G.1.4	Qualification (MD…….)	**Dr**
G.1.5	Professional address:	
G.1.5	Institution name	[redacted]

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

G.3	CENTRAL TECHNICAL FACILITIES TO BE USED IN THE CONDUCT OF THE TRIAL **Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised** (repeat as needed for multiple organisations).	
G.3.1	Name of organisation:	**LGC Axolabs**
G.3.2	Department	
G.3.3	Name of contact person:	
G.3.3.1	Given name	[redacted]
G.3.3.2	Middle name	
G.3.3.3	Family name	[redacted]
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No •**

G.3.8.2	Clinical chemistry	**No •**
G.3.8.3	Clinical haematology	**No •**
G.3.8.4	Clinical microbiology	**No •**
G.3.8.5	Histopathology	**No •**
G.3.8.6	Serology/ endocrinology	**No •**
G.3.8.7	Analytical chemistry	**No •**
G.3.8.8	ECG analysis/ review	**No •**
G.3.8.9	Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	**No •**
G.3.8.10	Primary/ surrogate endpoint test	**No •**
G.3.8.11	Other Duties subcontracted?	**Yes •**
G.3.8.11.1	If 'Yes', specify the other duties	**PK/PDM Bioanalysis**

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:	**PRA International**
G.3.2	Department	
G.3.3	Name of contact person:	
G.3.3.1	Given name	[redacted]
		[redacted]
		[redacted]
G.3.6	Fax number:	
G.3.7	E-mail:	
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No •**
G.3.8.2	Clinical chemistry	**No •**
G.3.8.3	Clinical haematology	**No •**
G.3.8.4	Clinical microbiology	**No •**
G.3.8.5	Histopathology	**No •**
G.3.8.6	Serology/ endocrinology	**No •**
G.3.8.7	Analytical chemistry	**No •**
G.3.8.8	ECG analysis/ review	**No •**
G.3.8.9	Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	**No •**
G.3.8.10	Primary/ surrogate endpoint test	**No •**
G.3.8.11	Other Duties subcontracted?	**Yes •**
G.3.8.11.1	If 'Yes', specify the other duties	**PK/PDM Concentration Bioanalysis**

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:	**Syneos Health**
G.3.2	Department	
G.3.3	Name of contact person:	
G.3.3.1	Given name	[redacted]
G.3.3.2	Middle name	
G.3.3.3	Family name	
G.3.4	Address:	
G.3.4.1	Street address	
G.3.4.2	Town/city	

G.3.4.3	Post code	[redacted]
[redacted]	[redacted]	
G.3.5	Telephone number:	
G.3.6	Fax number:	
G.3.7	E-mail:	
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No** •
G.3.8.2	Clinical chemistry	**No** •
G.3.8.3	Clinical haematology	**No** •
G.3.8.4	Clinical microbiology	**No** •
G.3.8.5	Histopathology	**No** •
G.3.8.6	Serology/ endocrinology	**No** •
G.3.8.7	Analytical chemistry	**No** •
G.3.8.8	ECG analysis/ review	**No** •
G.3.8.9	Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	**No** •
G.3.8.10	Primary/ surrogate endpoint test	**No** •
G.3.8.11	Other Duties subcontracted?	**Yes** •
G.3.8.11.1	If 'Yes', specify the other duties	**PK concentration data for ETV, TDF and TAF**

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:	**DDL Diagnostic Laboratory**
G.3.2	Department	
G.3.3	Name of contact person:	[redacted]
G.3.3.1	Given name	
G.3.3.2	Middle name	
G.3.3.3	Family name	
G.3.4	Address:	
G.3.4.1	Street address	
G.3.4.2	Town/city	
G.3.4.3	Post code	
G.3.4.4	Country	
G.3.5	Telephone number:	
G.3.6	Fax number:	
G.3.7	E-mail:	
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No** •
G.3.8.2	Clinical chemistry	**No** •
G.3.8.3	Clinical haematology	**No** •
G.3.8.4	Clinical microbiology	**No** •
G.3.8.5	Histopathology	**No** •
G.3.8.6	Serology/ endocrinology	**No** •
G.3.8.7	Analytical chemistry	**No** •
G.3.8.8	ECG analysis/ review	**No** •
G.3.8.9	Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	**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	**Clinical virology**

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:	**ABF Pharmaceutical Services GmbH (a member of the GBA Group Pharma)**

G.3.2	Department	
G.3.3	Name of contact person:	
G.3.3.1	Given name	
G.3.3.2	Middle name	
G.3.3.3	Family name	
G.3.4	Address:	
G.3.4.1	Street address	
G.3.4.2	Town/city	
G.3.4.3	Post code	
G.3.4.4	Country	
G.3.5	Telephone number:	
G.3.6	Fax number:	
G.3.7	E-mail:	
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No** •
G.3.8.2	Clinical chemistry	**No** •
G.3.8.3	Clinical haematology	**No** •
G.3.8.4	Clinical microbiology	**No** •
G.3.8.5	Histopathology	**No** •
G.3.8.6	Serology/ endocrinology	**No** •
G.3.8.7	Analytical chemistry	**No** •
G.3.8.8	ECG analysis/ review	**No** •
G.3.8.9	Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	**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	**Logistics and Isolation of PBMC samples**

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:	**Centrum voor Vaccinologie (CEVAC)**
G.3.2	Department	**University Hospital Ghent**
G.3.3	Name of contact person:	
G.3.3.1	Given name	
G.3.3.2	Middle name	
G.3.3.3	Family name	
G.3.4	Address:	
G.3.4.1	Street address	**laan**
G.3.4.2	Town/city	
G.3.4.3	Post code	
G.3.4.4	Country	
G.3.5	Telephone number:	
G.3.6	Fax number:	
G.3.7	E-mail:	
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No** •
G.3.8.2	Clinical chemistry	**No** •
G.3.8.3	Clinical haematology	**No** •
G.3.8.4	Clinical microbiology	**No** •
G.3.8.5	Histopathology	**No** •
G.3.8.6	Serology/ endocrinology	**No** •
G.3.8.7	Analytical chemistry	**No** •
G.3.8.8	ECG analysis/ review	**No** •
G.3.8.9	Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	**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	**Testing of PBMC samples**

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:	**CSM Europe sa**
G.3.2	Department	
G.3.3	Name of contact person:	
G.3.3.1	Given name	[redacted]
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No •**
G.3.8.2	Clinical chemistry	**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	**Long term storage of samples**

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:	**eResearch Technology, INC**
G.3.2	Department	
G.3.3	Name of contact person:	
G.3.3.1	Given name	
G.3.3.2	Middle name	
G.3.3.3	Family name	
G.3.4	Address:	
G.3.4.1	Street address	[redacted]
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**No •**
G.3.8.2	Clinical chemistry	**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	**Digital ECG Collection and Delivery**

G.4	**NETWORKS TO BE INVOLVED IN THE TRIAL (e.g. Paediatric Networks involved in the trial)**
G.4.1	Name of organisation:
G.4.2	Name of contact person:
G.4.2.1	Given name
G.4.2.2	Middle name
G.4.2.3	Family name
G.4.3	Address:
G.4.3.1	Street address
G.4.3.2	Town/city
G.4.3.3	Post code
G.4.3.4	Country
G.4.4	Telephone number:
G.4.5	Fax number:
G.4.6	E-mail:
G.4.7	Activities carried out by the network:

G.5	**ORGANISATIONS TO WHOM THE SPONSOR HAS TRANSFERRED TRIAL RELATED DUTIES AND FUNCTIONS**	
G.5.1	**Has the sponsor transferred any major or all the sponsor's trial related duties and functions to another organisation or third party?**	**Yes •**

Repeat as necessary for multiple organisations:

G.5.1.1	Organisation name:	**Signant Health**
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	
G.5.1.4.2	Town/city	
G.5.1.4.3	Post code	
G.5.1.4.4	Country	
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	
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:	**IWRS**

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:	**Imperial**
G.5.1.2	Organisation department	
G.5.1.3	Name of contact person :	[redacted]
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	
G.5.1.4.2	Town/city	
G.5.1.4.3	Post code	
G.5.1.4.4	Country	
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:	**Site and Patient facing material creation, translation, production, and shipping, archiving 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:	**Parexel International Corp**
G.5.1.2	Organisation department	
G.5.1.3	Name of contact person :	[redacted]
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	
G.5.1.4.2	Town/city	
G.5.1.4.3	Post code	
G.5.1.4.4	Country	
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	**Yes •**
G.5.1.14	E-data capture	**No •**
G.5.1.15	SUSAR reporting	**No •**
G.5.1.16	Quality assurance auditing	**No •**
G.5.1.17	Statistical analysis	**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:	**SGS**
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	
G.5.1.4.2	Town/city	
G.5.1.4.3	Post code	
G.5.1.4.4	Country	
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	
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:	**PK and SD Office 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:	**Medidata Solutions**
G.5.1.2	Organisation department	
G.5.1.3	Name of contact person :	
G.5.1.3.1	Given name	

G.5.1.4	Address:	
G.5.1.4.1	Street address	[redacted]
G.5.1.6	Fax number:	
G.5.1.7	E-mail:	[redacted]
G.5.1.8	All tasks of the sponsor	**No** •
G.5.1.9	Monitoring	**No** •
G.5.1.10	Regulatory (e.g. preparation of applications to CA and ethics committee)	**No** •
G.5.1.11	Investigator recruitment	**No** •
G.5.1.12	IVRS[30] – treatment randomisation	**No** •
G.5.1.13	Data management	**No** •
G.5.1.14	E-data capture	**Yes** •
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:	

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:	**Unknown**
H.2.2	Address	
H.2.2.1	Street address	
H.2.2.2	Town/city	
H.2.2.3	Post code	
H.2.2.4	Country	
H.2.3	Date of submission:	

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

I. SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

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

I.2	**APPLICANT OF THE REQUEST FOR THE COMPETENT AUTHORITY** (as stated in section C.1):
I.2.1	Date:
I.2.2	Signature[31]: [redacted]
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.