To:

All Member States participating in EFC17561

21-Feb-2024

Product Code/Name: SAR445229 / Amlitelimab

Protocol Code: EFC17561

Protocol Title: A Phase 3, randomized, double-blind, placebo-controlled, parallel group, 3-arm, multinational, multicenter study to evaluate the efficacy and safety of amlitelimab by subcutaneous injection in participants aged 12 years and older with moderate to severe atopic dermatitis on background topical corticosteroids.

Universal trial number: U1111-1275-9760

EU trial number: 2023-506558-20

Subject: Clinical Trial Application - Request for Initial authorization

Dear Madam, Dear Sir,

Sanofi-Aventis Research & Development hereby submits a Clinical Trial Application for the Clinical Study EFC17561.

This is a parallel group, Phase 3, multinational, multicenter, randomized, double-blind, placebo-controlled, 3-arm study for treatment of participants diagnosed with moderate-to-severe atopic dermatitis (AD) with a history of inadequate response of topical treatment, on background topical corticosteroid (TCS) and/or topical calcineurin inhibitor (TCI).

The purpose of this study is to measure the efficacy and safety of treatment with amlitelimab solution for subcutaneous (SC) injection compared with placebo in participants with moderate to severe AD aged 12 years and older on background TCS and/or TCI.

In terms of specific vulnerable populations, women of childbearing potential using contraception and Participants incapable of giving consent personally will be included.

Please note that EFC17561 is included as part of the PIP (Pediatric investigational plan number: EMEA-003233-PIP01-22).

In a 6 month juvenile toxicology study in 11 to 15 months old monkey, amlitelimab did not induce any effect on bone turnover biomarkers, on microscopic evaluation of growth plates or in bone micro-CT parameters. The NOEL was the highest dose level tested, 50 mg/kg/week SC. These findings support

the lack of impact of amlitelimab on bone growth and further supports the inclusion of pediatric patients in the clinical development plan. An IB edition 8 will be updated to include the findings from the completed 6-month juvenile toxicology study in the next annual update expected in Q2 2024 and will be submitted to the HA.

We propose Germany as the Reporting Member State.

The following countries are proposed to take part in the study:

- Bulgaria
- Czechia
- France
- Germany
- Italy
- Spain

The anticipated date of the next DSUR submission is: 08-Jun-2024

For administrative information, please see Administrative information.

For any additional information, please see Specificities.

Should you have any queries on the enclosed, please do not hesitate to contact us

Yours sincerely,

Sanofi-Aventis Research & Development

Administrative information

Information		**Location of the Information in the Application Dossier**
Proposed Reporting Member State	Germany	Not Applicable
Specific features of the clinical trial population	☒ Subjects not able to give informed consent ☒ Minors ☐ Pregnant or breastfeeding women ☐ None of the above	Please refer to Structure Data in the Part I \ Trial details \ Trial information \ Population of trial subjects
Does the clinical trial involve the first administration of a new active substance to humans?	☐ Yes ☒ No	Not Applicable
Has a scientific advice relating to the clinical trial or the investigational medicinal product SAR445229 been given by the Agency, a Member State or a third country?	☒ Yes ☐ No	Please refer to Structure Data in the Part I \ Trial details \ Scientific advice and Paediatric Investigation Plan (PIP)
Is the clinical trial part or will it be part of a Paediatric Investigation Plan (PIP)?	☒ Yes ☐ No	Please refer to Structure Data in the Part I \ Trial details \ Scientific advice and Paediatric Investigation Plan (PIP)
Has the investigational medicinal product SAR445229 obtained an orphan designation?	☐ Yes ☒ No	Please refer to Structure Data in the Part I \ Products \ SAR445229 \ Orphan Designation
Is the clinical trial considered by the sponsor to be a low-intervention clinical trial?	☐ Yes ☒ No	Please refer to Structure Data in the Part I \ Trial details \ Trial information \ Trial Category
Does the methodology of the clinical trial require that groups of subjects rather than individual subjects are allocated to receive different investigational medicinal products in a clinical trial? If Yes, will the informed consent be obtained by simplified means?	☐ Yes ☒ No ☐ Yes ☐ No	

The Investigational Medicinal Product in this clinical study is:

Investigational Medicinal Product	Regulatory status	Reference Safety Information localisation	Additional information
SAR445229 / Amlitelimab	☐ Approved in the EU ☒ Not Approved in the EU	- section 8 (Reference safety information for assessment of expectedness of serious adverse reactions) of the Investigator's Brochure	Is the IMP a: - narcotic: ☐ Yes ; ☒ No - psychotropic: ☐ Yes ; ☒ No -radiopharmaceutical: ☐ Yes ; ☒ No (Please refer to Structure Data in the Part I \ Products \ SAR445229 \ Product characteristics) Does the IMP consist of or contain a genetically-modified organism or organisms? ☐ Yes ; ☒ No (Please refer to Structure Data in the Part I \ Products \ SAR445229 \ Advanced Therapy Medicinal Product)

The auxiliary medicinal products in this clinical study are:

Auxiliary medicinal product	Regulatory status	Additional information
Topical Corticosteroids-rescue medications D07A	☒ Approved in the EU ☐ Not Approved in the EU	Sourcing by the site/patient: France, Germany, Czechia, Spain, Italy, Bulgaria
Topical Corticosyeroids- background therapy D07A	☒ Approved in the EU ☐ Not Approved in the EU	Sourcing by the site/patient: France, Germany, Czechia, Spain Sourcing by/on behalf of the Sponsor: Italy, Bulgaria
Topical calcineurin inhibitors – background therapy -D11AH01 (tacrolimus) -D11AH02 (pimecrolimus)	☒ Approved in the EU ☐ Not Approved in the EU	Sourcing by the site/patient: France, Germany, Czechia, Spain Sourcing by/on behalf of the Sponsor: Italy, Bulgaria

The medical devices which are to be investigated in this clinical trial but which are not part of the investigational medicinal product or products are:

Medical device	Additional information
No medical devices are being investigated as part of the clinical trial.	The amlitelimab prefilled syringe (PFS) is classified as a medicinal product combined with an integral medical device where the principal mechanism of action is that of the medicinal product. The combined product is governed by the medicines legislation and a CE mark is not applicable. For these combined products, the requirements of article 117 of the Regulation (EU) 2017/745 must be taken into account at the time of a marketing authorization application. In accordance with the requirements for clinical use of prefilled syringe, Sanofi certifies that the amlitelimab prefilled syringe used in context of the clinical trial is in compliance with the relevant general safety and performance requirements defined in Annex I of Regulation (EU) 2017/745 and every precaution has been taken to protect the health and safety of patients. The PFS is merely the delivery system for the medicinal product and is not being investigated as part of the clinical trial, nor are there clinical claims associated with the PFS
No IVD medical device are being used for investigational purposes during the course of this study.	All IVD medical devices are CE-marked for its analytical validation and will be used per its IFU. List of IVD medical device has been included below.

Test Name	MTM#	CE-marked IVD assay/platform being used?
Partial Thromboplastin Time, Activated (APTT)	782	CE
Prothrombin Time (PT)	780	CE
Prothrombin Time, International Normalized Ratio (INR)	781	CE
Chemistry Panel		
Albumin	1	CE
Alkaline Phosphatase (ALP)	7918	CE
Alanine Aminotransferase (ALT)	13	CE
Aspartate Aminotransferase (AST)	33	CE
Bicarbonate (Carbon Dioxide)	46	CE
Bilirubin, Direct	48	CE
Bilirubin, Total	49	CE
Calcium	54	CE
Chloride	58	CE
Creatine Phosphokinase (CPK)	68	CE
Creatinine	69	CE
Gamma Glutamyl Transferase (GGT)	109	CE
Glucose	112	CE
Glucose, Random	10738	CE
Lactate Dehydrogenase (LDH)	153	CE
Phosphorous	211	CE
Potassium	215	CE
Protein	221	CE
Sodium	242	CE
Urea, Blood Nitrogen (BUN)	272	CE

Estimated Glomerular Filtration Rate (eGFR) (CKD-EPI 2021)	55119	calculation
HCG (Human Chorionic Gonadotropin)	2395	CE
HCG (Human Chorionic Gonadotropin)	1821	CE
Follicle Stimulating Hormone (FSH)	2401	CE
Hepatitis B, Surface Antigen Panel		
Hepatitis B, Surface Antigen	2406	CE
Hepatitis B, Surface Antigen Confirmation	2407	CE
Hepatitis B, Surface Antibody Total	2405	CE
Hepatitis B, Core Antibody, IgM	2403	CE
Hepatitis B, Core Antibody, Total	2404	CE
Hepatitis C, Antibody, IgG	2408	CE
Human Immunodeficiency Virus, Types 1 & 2 (HIV 1&2)	2426	CE
Hepatitis C Virus (HCV) Viral Load, Qualitative (Cobas 6800)	63389	CE
HIV 1 & 2 Geenius Differentiation and Confirmation	15919	CE
Hepatitis B Virus (HBV) Viral Load, Qualitative (Cobas 6800)	63725	CE
Allergen Total IgE	3281	CE
Quantiferon Plus TB Panel		
Quantiferon TB Plus, Nil Tube	13760	CE
Quantiferon TB Plus, Antigen Tube 1	13719	CE
Quantiferon TB Plus, Antigen Tube 2	13739	CE
Quantiferon TB Plus, Mitogen Tube	13759	CE
CBC Auto Diff Panel		
CBC, Hematocrit (Hct)	9638	CE
CBC, Hemoglobin (Hgb)	9639	CE
CBC, Red Blood Cell (RBC)	9558	CE
CBC, White Blood Cell (WBC)	9679	CE
CBC, Platelet Count (PLT)	9660	CE
CBC, Mean Corpuscular Hemoglobin (MCH)	9658	CE
CBC, Mean Corpuscular Hemoglobin Concentration (MCHC)	9640	CE
CBC, Mean Corpuscular Volume (MCV)	9659	CE
CBC, Mean Platelet Volume (MPV)	9641	CE
CBC, Red Cell Distribution Width (RDW)	9678	CE
CBC, Nucleated Red Blood Cell (NRBC %)	11662	CE
CBC, Nucleated Red Blood Cell (Absolute) (NRBC)	9700	CE
WBC Differential, Basophils	10202	CE
WBC Differential, Basophils (Absolute Count)	10201	CE
WBC Differential, Eosinophils	10203	CE
WBC Differential, Eosinophils (Absolute Count)	10218	CE
WBC Differential, Immature Granulocyte	10239	CE
WBC Differential, Immature Granulocytes (Absolute Count)	10238	CE
WBC Differential, Lymphocytes	10240	CE
WBC Differential, Lymphocytes (Absolute Count)	10258	CE
WBC Differential, Monocytes	10241	CE
WBC Differential, Monocytes (Absolute Counts)	10278	CE
WBC Differential, Neutrophils (Sysmex)	10243	CE
WBC Differential, Neutrophils (Sysmex, Absolute Count)	10242	CE
Urinalysis Macroscopic Panel		
Urinalysis, Automated, Bilirubin	9081	CE
Urinalysis, Automated, Blood	9138	CE

Urinalysis, Automated, Glucose	9258	CE
Urinalysis, Automated, Ketone	9278	CE
Urinalysis, Automated, Leukocyte Esterase	9298	CE
Urinalysis, Automated, Nitrite	9318	CE
Urinalysis, Automated, pH	9341	CE
Urinalysis, Automated, Protein	9338	CE
Urinalysis, Automated, Specific Gravity	9339	CE
Urinalysis, Automated, Urobilinogen	9340	CE
Urinalysis Microscopic Panel – Automated		
Urinalysis, Microscopic, Amorphous Crystals	306	CE
Urinalysis, Microscopic, Bacteria	34	CE
Urinalysis, Microscopic, Calcium Carbonate Crystals	308	CE
Urinalysis, Microscopic, Calcium Oxalate Crystals	310	CE
Urinalysis, Microscopic, Calcium Phosphate Crystals	312	CE
Urinalysis, Microscopic, Cysteine Crystals	314	CE
Urinalysis, Microscopic, Granular Casts	329	CE
Urinalysis, Microscopic, Hyaline Casts	331	CE
Urinalysis, Microscopic, Leucine Crystals	316	CE
Urinalysis, Microscopic, Mucus	339	CE
Urinalysis, Microscopic, RBC	468	CE
Urinalysis, Microscopic, Red Blood Cell Casts	333	CE
Urinalysis, Microscopic, Renal Epithelial Cells	341	CE
Urinalysis, Microscopic, Squamous Epithelial Cells	343	CE
Urinalysis, Microscopic, Transitional Epithelial Cells	345	CE
Urinalysis, Microscopic, Triple Phosphate Crystals	318	CE
Urinalysis, Microscopic, Tyrosine Crystals	320	CE
Urinalysis, Microscopic, Uric Acid Crystals	322	CE
Urinalysis, Microscopic, Waxy Casts	335	CE
Urinalysis, Microscopic, WBC	470	CE
Urinalysis, Microscopic, White Blood Cell Casts	337	CE
Urinalysis, Microscopic, Yeast	347	CE
SARS CoV-2 Assay (Qualitative)	62029	CE

Specificities

Germany:

Local pre-Scientific Advice meeting according to KBPV not to take place in Germany

Radiation protection assessment by Ethics Committee is not required in Germany

Italy:

The proposed Ethics Committee for Italy is:

Comitato Etico Territoriale Lombardia 3

Email: federica.massacesi@policlinico.mi.it

"Stamp duty virtually paid pursuant to Art. 15 of DPR 642 of 26.10.1972, authorization no. 267351 of 9.11.2020 issued by the Revenue Agency, provincial direction of Milan 2"

Spain:

The proposed Ethics Committee for Spain is:

Comité de Ética de la Investigación con Medicamentos La Paz
Paseo de la Castellana, 261
Madrid
28046

REec User: es-reg-estudiosclinicos@sanofi.com