R&D For Unmet Needs & Patent Management

GRI Standards:

N/A

R&D For Unmet Needs and Patent Management – Develop new solutions for patients and manage patents responsibly.

R&D For Unmet Needs

Innovation is the essence of the research-based pharmaceutical industry. Developing a new medicine takes, on average, ten to 13 years, with costs ranging from U.S. $2.5-3.0 billion (including costs of failures) with about 12% of drugs entering clinical trials leading to an approved medicine. Over the last decades, Sanofi has demonstrated our sustained contribution to global health challenges by developing a large portfolio of solutions for a wide range of diseases that affect millions of people globally.

As part of our commitment to society, we consider it essential to identify how our science can bring the greatest benefit, especially for vulnerable communities. We have therefore integrated a specific pillar into our CSR strategy, which addresses R&D for unmet needs.

Contribute to sleeping sickness disease elimination in 2030

Sanofi has collaborated with the World Health Organization (WHO) since 2001, with the objective of contributing to eliminate sleeping sickness, or Human African Trypanosomiasis (HAT), by 2030. Sleeping sickness is a Neglected Tropical Disease, which affects mostly poor populations living in remote rural areas of sub-Saharan Africa. If left untreated, the parasitic disease is usually fatal. Since the start of Sanofi's collaboration with the WHO, the number of cases of sleeping sickness has fallen by 97%, from 26,950 in 2001 to 837 in 2022, dropping below 1,000 for the fifth consecutive year.

Sanofi is engaged in supplying drugs and vaccines and contributing to the definition and implementation of public health policy beyond where market forces work through partnerships. We have a long-term partnership with the Drugs for Neglected Diseases initiative (DNDi) to develop a new all-oral monotherapy, fexinidazole, which was first approved at the end of 2018 in the Democratic Republic of Congo (DRC). While previous treatments required long hospitalizations and intravenous administration, this new, all-oral monotherapy reduces treatment to a ten-day once-a-day treatment that is effective in both the first and the second stages of the disease in adults and children aged six years and older and weighing 20 kg or more. Fexinidazole also received WHO prequalification in March 2019, and was approved in Uganda and the United States in 2021. It has been included in the WHO Essential Medicines List and WHO sleeping sickness treatment guidelines, as a first-line treatment for first stage and non-severe second stage. Very recently, the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has extended the indication of fexinidazole for the treatment, in patients suffering Trypanosoma brucei (T.b.) rhodesiense sleeping sickness, an acute and lethal form of this parasitic disease found in Eastern and Southern Africa. This is the first full oral treatment for these patients whose only option previously had been an arsenic-based treatment.

In September 2020, Sanofi and DNDi signed an agreement to develop and roll out acoziborole, a second innovative sleeping sickness treatment. Once approved, the treatment could be administered in a single dose at the point of diagnosis making it a game-changer to support the sustainable elimination of the disease. This new chemical entity has been tested in Phase II/III clinical studies in DRC and Guinea. The results, which were published in The Lancet Infectious Diseases medical journal in November 2022, showed that the 18-month treatment success rate for acoziborole was 95% in late-stage Trypanosoma brucei gambiense (g-HAT patients), corresponding to the best results from studies with existing treatments (94%). In addition, 100% of the 41 patients with earlystage g-HAT were considered as treatment successes at all timepoints. The study shows that acoziborole has a favorable safety profile, with no significant drug-related safety signals being reported. These pivotal results will form the basis of Sanofi's dossier submission to the European Medicines Agency (EMA), and represent another milestone in the quest to eliminate sleeping sickness.

Through Sanofi's partnership with the World Health Organization (WHO), the company supports disease management, including screening of populations, disease awareness campaign, capacity building, and drug donation. At the end of 2023, Sanofi's total contribution to this WHO program was $115 million. The partnership agreement was renewed in 2020 for another five years, with a commitment to contribute $5 million annually from Sanofi. The program includes controls over the quality and use of the products, as well as distribution, which is handled jointly with Médecins Sans Frontières (MSF). This long-term commitment is key to achieving the sustainable elimination of sleeping sickness by 2030, as per the WHO Neglected Tropical Disease roadmap.

As of October 2022, the Neglected Tropical Diseases program is managed by Foundation S – the Sanofi Collective. Foundation S is committed to donate acoziborole until sleeping sickness is eliminated worldwide.

Develop innovative treatments for childhood cancer

Cancer remains the leading cause of death from disease in children in the developed world, and most of the medicines we use to treat childhood cancer today were approved decades ago. While some progress has been made in improving survival rates for certain types of childhood cancer, there remains an unmet medical need, with many survivors experiencing severe long-term side effects. Developing innovative treatments for childhood cancers is challenging due to their rarity and regulatory concerns, resulting in significant delays in making new therapies available for children. The median time between the first adult trial and the first child trial is currently 6.5 years. As part of its CSR strategy, Sanofi is committed to addressing childhood cancer through a three-pillar approach:

1. Developing innovative treatments: Sanofi aims to develop highly effective and safe treatments to improve outcomes for children with cancer and to reduce clinical trial delays for children. Leveraging its R&D capabilities, Sanofi focuses on its late research and early development pipeline for the timely completion of preclinical studies and the initiation of clinical trials. In November 2023, Sanofi was therefore able to dose the first pediatric patient with one of its assets, less than two years after this same asset had been dosed in the first adult patient.

2. Closing knowledge gaps: Sanofi's second pillar focuses on better understanding childhood cancer and its resistance to standard treatments. This involves leveraging internal programs like the Sanofi i-awards for which a first dedicated project for childhood cancer was selected in in November 2023. Sanofi also engages in partnerships with experts from renowned institutions, and with consortia. Partnerships engaged in since 2021 include those with experts from the MD Anderson Cancer Center and with institutions like the Innovative Therapies for Children with Cancer (ITCC) consortium, the Innovative Therapies for Children with Cancer's Pediatric Preclinical Proof of Concept Platform (ITCCP4), and the FNIH Convening Experts in Oncology to Address Children's Health (COACH). In September 2023, Sanofi and ITCC/Institut Gustave Roussy started building a multi-stakeholder Childhood Cancer Working Group at the Paris Saclay Cancer Cluster (PSCC) to tap into PSCC's impressive infrastructure (data, samples, models) and propose relevant research projects.

3. Raising awareness: We collaborate with patient advocacy groups (e.g. MIB Agents and Imagine for Margo) to embed patient insights into healthcare solutions, and participating in various awareness initiatives including symposia, webinars, and training courses. Sanofi's childhood cancer project team works closely with the Foundation S My Child Matters project team.

Develop Global Access Plans for our innovation pipeline

In parallel with our efforts to enhance patient access to our existing medicines and vaccines, we are also committed to accelerating broader patient access to our future innovations by developing Global Access Plans (GAPs) at an early stage of clinical development for all our R&D pipeline assets.

Our ambition is to make our innovative products available within two years after first launch wherever we can make an impact on patients, and when external conditions allow. This ambition was shared in a public announcement made in 2021 as part of our renewed commitment to society. Our GAPs systematically explore the opportunity for establishing access models and conditions as early as Phase II, after proof of concept (POC), in order to consider all potential solutions for broader patient access at scale beyond the usual commercial approaches in baseline countries :

- focusing on geographies where a significant unmet medical need remains, and the healthcare ecosystem can support safe integration of innovations into clinical practices;
- adapting actions alongside the value chain: R&D, manufacturing and supply, regulatory pathways, pricing and reimbursement conditions, as well as building health system infrastructure and capabilities to ensure patients have effective access to care and appropriate use of our products; and
- developing access models adapted to local specificities.

The responsibility for developing a GAP lies in the business units for their respective assets, including key global functions and markets specialists, and GAPs are fully embedded in the global brand strategy. Our methodology enables the business to define which assets or countries to prioritize, and which offering is best suited for these assets and geographies. The methodology includes all the steps, implications, and issues to solve alongside the value chain including R&D, and more particularly clinical trial site localization; manufacturing and supply; regulatory pathways; legal considerations; healthcare capability-building; and the go-to-market model.

As of December 2023, 8 Global Access Plans have been initiated or developed, covering more than 12 indications. Sanofi will continue to develop GAPs for future assets when they reach Phase II of clinical development.

Patent Management

Intellectual property rights established by the World Trade Organization have performed a critical role in stimulating R&D. By sharing risks and rewards, this system has created the appropriate environment for delivering the greatest returns for society not just for today, but also for tomorrow.

Sanofi believes that patents are a fundamental incentive for driving innovation in the pharmaceutical sector. The development of new medicines and vaccines is a risky, costly, and lengthy process. Patents are an essential incentive for pharmaceutical companies to invest in research & development to address unmet medical needs. IP policies therefore need to be safeguarded. While patents by themselves should not be considered a barrier for access, Sanofi believes that being transparent and flexible with our patents can help address pressing health challenges in developing countries.

In order to enable access to our medicines and vaccines:

- Sanofi makes patent status of their Essential Medicines and Vaccines in developing countries publicly available (see Annex I);
- Sanofi does not file patent applications or enforce patent rights in all Least Developed Countries (LDCs) and Low-Income Countries (LICs);
- Sanofi does not file or enforce patents in several Lower-Middle-Income Countries (LMICs) and Upper-Middle-Income Countries (UMICs). See Annex II for the complete list of countries;
- Sanofi supports implementation of the 2001 WTO Doha Declaration on TRIPS and Public Health and the appropriate use of the flexibilities therein intended to protect public health;
- Sanofi supports the transition period that LDCs are exempted from obligations under the Agreement on Trade Relate Aspects of Intellectual Property Rights (TRIPS Agreement) regarding pharmaceutical patents until January 1, 2033. We support this exemption of LDCs and an extension of the exemption beyond 2033;
- Sanofi acknowledges the value of voluntary licensing agreements and patent pools for access to medicines in developing countries. We would consider joining patent pools and engaging in voluntary licensing if relevant to our portfolio, and aimed at accelerating access to medicines and vaccines in low- and middle- income countries;
- Sanofi respects compulsory licensing as a short-term and targeted measure where urgent access to patented medicines is critical to maintaining public health, and no appropriate alternative is available. We believe that compulsory licenses should only be used in extraordinary and very limited circumstances, such as meeting a health crisis or emergency; and
- Sanofi respects a formal exemption from patent infringement for activities which are undertaken as part of the regulatory review process: "[c]onducting the necessary studies and trials with a view to the application of paragraphs 1 to 4 [i.e. bioequivalents and biosimilars] and the consequential practical requirements shall not be regarded as contrary to patent rights or to supplementary protection certificates for medicinal products." (Bolar exemption, Directive 2004/27/EC. Article 10(6)).

Annex I - Patent Status of Sanofi's Essential Medicines and Vaccines in Developing Countries

Annex II - Developing Countries in which Sanofi does not file or enforce patents*

* For products where Sanofi solely owns and controls the patent rights

Annex I: Sanofi Products[1] as of 2023 listed on the WHO Essential Medicine List (EML, 2023)

MEDICINES		
Product	**Active Ingredient(s)**	**Patent Rights**
AGEN®	Amlodipine	No
APPROVEL®	Irbesartan[2]	No[4]
ARSOBAL®	Melarsoprol	No
ASAQ Winthrop®	Artesunate/ amodiaquine	No
AZITRHOMYCIN	Azithromycin dihydrate	No
BLEOMYCINE	Bleomycin	No
CAPTEA	Captopril/Hydrochlorothiazide	No
CERUBIDINE®	Daunorubicin	No
CETAPIN®	Metformin hydrochloride	No
CIDOMYCIN®	Gentamicin	No
DEPAKINE®	Valproate sodium	No
EFAVIRENZ	Efavirenz	No
ELOXATIN®	Oxaliplatin	No
ENOXAPARIN	Enoxaparin	No
ERYTHROMYCIN	Erythromycin	No
EURELIX	Piretanide	No
FEXINIDAZOLE Winthrop	Fexinidazole	No [3]
FLAGYL®	Metronidazole benzoate	No
FLUDARA®	Fludarabine phosphate	No
GARDENAL®	Phenobarbital	No
GLUCANTIME®	Meglumine antimoniate	No
ISONIAZID	Isoniazid	No
LANTUS®	Insulin glargine	No [4]
MALOCIDE®	Pyrimethamine	No
PENTACARINAT®	Pentamidine	No
PLAVIX®	Clopidogrel	No
PRIFTIN®	Rifapentine	No
PRIMAQUINE	Primaquine diphosphate	No
PYRAZINAMIDE	Pyrazinamide	No
QUINIMAX®	Quinine	No
RIFADIN®	Rifampicin	No
RIFATER®	Rifampicin/ isoniazid/ pyrazinamide	No
RIFINAH®	rifampicin/ isoniazid	No
RISORDAN®	Isosorbide dinitrate	No
STEMETIL®	Prochlorperazine mesilate[2]	No
TAVANIC®	Levofloxacin	No
TAXOTERE®	Docetaxel	No
TENOFOVIR	Tenofovir disoproxil	No
TERCIAN	Cyamemazine	No
TRITAZIDE®	Ramipril/Hydrochlorothiazide	No
TRIAPIN®	Ramipril/Felodipine	No
VERAPAMIL	Verapamil	No

VACCINES		
Product	**Vaccine Type**	**Patent Rights**
ACTHIB®	*Haemophilus influenzae* polysaccharide type b conjugated to tetanus protein (PRP-T)	No
ADACEL®	Diphtheria, Tetanus, Pertussis (acellular, component) Vaccine (adsorbed, reduced antigen(s) content)	No
DENGVAXIA®	Dengue live attenuated tetravalent chimeric vaccine	No [5]
HEXAXIM®	Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated) and *Haemophilus influenzae* type b conjugate vaccine (adsorbed)	No [6]
MENACTRA®	Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine	No [6]
PENTAXIM®	Diphtheria, tetanus, pertussis (acellular, component), poliomyelitis (inactivated) vaccine and *Haemophilus* type b conjugate vaccine, adsorbed	No
STAMARIL	Yellow Fever Vaccine	No
TETAVAX®	Purified tetanus toxoid (PTT)	No
TETRAXIM®	Booster vaccine	No

TYPHIM VI®	Typhoid polysaccharide vaccine	No
VAXIGRIPTETRA®	Quadrivalent influenza vaccine (split virion, inactivated)	No
VAXIGRIP®	Influenza vaccine (split virion, inactivated)	No
VERORAB®	Rabies vaccine, inactivated	No

DEVICES FOR LANTUS ADMINISTRATION		
Product		**Patent Rights**
ALLSTAR®	Reusable pen	No (4)
SOLOSTAR®	Prefilled pen	No (4)

(1) Sanofi products encompass the products marketed and/or distributed in 2023 by Sanofi and its affiliates. Trademarks followed with ® mean that the trademark is registered in one or some of the countries listed in Annex II. Depending on the countries, (i) some products are associated with other trademarks, not listed in Annex I and (ii) some trademarks are used under licensing by Sanofi. FLUDARA® is a registered trademark of Alcafleu. TAVANIC® is a registered trademark of Daiichi Sankyo limited. CETAPIN® and CIDOMYCIN® are registered in countries other than those listed in Annex II.

(2) Products followed with (2) are considered clinically equivalent medicines to a representative example within a pharmacological class listed on the 2021 WHO EML, as indicated by the square box symbol. All other products are listed on the 2021 WHO EML as core essential medicines.

(3) For countries via ARIPO, actions have been taken in June 2020 to effectively abandon patents directed to Fexinidazole. Therefore, the "no patent" statement applies to the product FEXINIDAZOLE Winthrop for countries listed in Annex II.

(4) The "no patent" statement applies to the products for countries listed in Annex II.

(5) For Lao, action has been taken in July 2021 to effectively abandon the patent covering DENGVAXIA®. Therefore, the "no patent" statement applies to the product DENGVAXIA® for countries listed in Annex II.

(6) For Syria, Tajikistan and countries via **ARIPO** or via **OAPI**, actions have been taken in November 2019 to effectively abandon patents or patent applications directed to HEXAXIM® or MENACTRA®. Therefore the "no patent" statement applies to the products HEXAXIM® and MENACTRA® for countries listed in Annex II.

For all other products listed with no patent in the present Annex I, this statement applies for countries listed in Annex II and for all other countries worldwide.

KEYS

ARIPO. 'African Regional Intellectual Property Organization' Countries:

Botswana; Gambia; Ghana; Kenya; Lesotho; Liberia; Malawi; Mozambique; Namibia; Rwanda; Sierra Leone; Sudan; Swaziland; Tanzania; Uganda; Zambia and Zimbabwe.

OAPI. 'Organisation Africaine de la Propriété Intellectuelle' Countries:

Benin; Burkina Faso; Cameroon; Central African Rep.; Chad; Comoros; Congo, Rep.; Côte d'Ivoire; Equatorial Guinea; Gabon; Guinea; Guinea-Bissau; Mali; Mauritania; Niger; Senegal and Togo.

Annex II

Developing Countries in Which Sanofi Does not File or Enforce Patent

Country	UN Classification (Sept. 2021)	World Bank Classification (July 2023)
Micronesia, Fed. Sts.	NO	LMIC
Cambodia	LDC	LMIC
Kiribati	LDC	LMIC
Korea, Dem. Rep	NO	LIC
Lao PDR	LDC	LMIC
Myanmar	LDC	LMIC
Mongolia	NO	LMIC
Papua New Guinea	NO	LMIC
Solomon Islands	LDC	LMIC
Timor-Leste	LDC	LMIC
Tonga	NO	UMIC
Tuvalu	LDC	UMIC
Vanuatu	NO	LMIC
Samoa	NO	LMIC
Tajikistan	NO	LMIC
Belize	NO	UMIC
Guyana	NO	HIC
Haiti	LDC	LMIC
Suriname	NO	UMIC
Djibouti	LDC	LMIC
Iraq	NO	UMIC
Palestine, State of (West Bank and Gaza)	NO	UMIC
Syrian Arab Rep.	NO	LIC
Yemen, Rep.	LDC	LIC
Afghanistan	LDC	LIC
Bangladesh	LDC	LMIC
Bhutan	LDC	LMIC
Maldives	NO	UMIC
Nepal	LDC	LMIC
Angola	LDC	LMIC
Burkina Faso	LDC	LIC
Burundi	LDC	LIC
Benin	LDC	LMIC
Botswana	NO	UMIC
Congo, Dem. Rep.	LDC	LIC
Central African Rep.	LDC	LIC
Congo, Rep.	NO	LMIC
Côte d'Ivoire	NO	LMIC
Cameroon	NO	LMIC
Cape Verde	NO	LMIC
Eritrea	LDC	LIC
Ethiopia	LDC	LIC
Gabon	NO	UMIC
Ghana	NO	LMIC
Gambia, The	LDC	LIC
Guinea	LDC	LMIC
Equatorial Guinea	NO	UMIC
Guinea-Bissau	LDC	LIC
Comoros	LDC	LMIC
Liberia	LDC	LIC
Lesotho	LDC	LMIC
Madagascar	LDC	LIC
Mali	LDC	LIC
Mauritania	LDC	LMIC
Malawi	LDC	LIC
Mozambique	LDC	LIC
Namibia	NO	UMIC
Niger	LDC	LIC
Rwanda	LDC	LIC
Sudan	LDC	LIC
Sierra Leone	LDC	LIC
Senegal	LDC	LMIC
Somalia	LDC	LIC
South Sudan	LDC	LIC
São Tomé and Principe	LDC	LMIC
Swaziland (Eswatini)	NO	LMIC
Chad	LDC	LIC
Togo	LDC	LIC
Tanzania	LDC	LMIC
Uganda	LDC	LIC
Zambia	LDC	LMIC
Zimbabwe	NO	LMIC

LDC: Least Developed Country, UN Human Development Index, September 2021.
LIC: Low Income Country, World Bank income classifications, July 2023.
LMIC: Lower middle-income country, World Bank income classifications, July 2023.

UMIC: Upper middle-income country, World Bank income classifications, July 2023