Sustainability Infosheet 2022

Product innovation

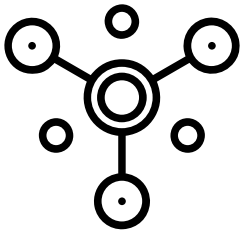
idorsia

Product innovation management approach

At Idorsia, we aim to deliver new products that have the potential to significantly change the treatment options in target diseases. This puts innovation at the heart of what we do. Our highly efficient innovation process spans all stages, from the discovery of a promising compound to the final commercialization of the drug. This cycle involves multiple departments, generating the information required by health authorities worldwide.

Idorsia's Scientific Board is responsible for making science-based strategic decisions across our drug discovery and clinical development pipeline, including projects from Phase 0 through Phase 3 of the pharmaceutical development lifecycle. The Board conducts an annual review of Idorsia's innovation pipeline and aligns priorities across global clinical development and drug discovery. The Board is composed of senior scientific leaders from across the company, including the Chief Scientific Officer; the Head of Global Clinical Development; the Head of Drug Discovery, Pharmacology and Preclinical Development; and the Chief Medical Officer. Other members of the Scientific Board from our research, clinical development, finance and commercial organizations are invited to attend meetings according to the topic and relevance for their role. The Scientific Board reports to the Idorsia Executive Committee.

Innovation from bench to bedside



Our innovation starts with a brilliant idea and culminates, we hope, in a new drug that can change the treatment paradigm in the target indication.

Drug discovery

Idorsia's drug discovery focuses on families of proteins, characterized by the way they work. We pursue innovative programs involving proteins which have not been targeted up to now, so as to develop drugs with novel mechanisms of action. We are also constantly looking for ways to integrate new technologies and approaches to drug design, such as the use of artificial intelligence (AI) tools.

The drug discovery process starts with an idea from our scientists. We scour the literature to see what others have not yet discovered, to generate ideas and then translate them into a concept which can lead to new treatments for patients.

Our work in the lab begins with the target. This may be a particular protein which, when its activity is modulated, can normalize a biological process in the body – with beneficial effects for patients. To see whether we can affect the protein's activity, we first need to be able to measure it.

We produce, or "express", the target in large quantities and measure its natural activity in assays. The assay needs to be sensitive, accurate and highly reliable. Plus, in order to perform hundreds of thousands of measurements, it needs to be automated, using robotic equipment.

But there are two sides to the discovery process – a target and a compound. Compounds are substances which, we hope, will modify the activity of a target involved in a pathological process and which can be developed into a drug for patients.

At Idorsia, we maintain a library consisting of hundreds of thousands of different compounds. To begin our hunt for drugs, we test the entire library on the target, in the hope that one of these compounds will modify the activity of the protein. This process is called high-throughput screening; if it's a simple assay, we can test the whole library within a matter of weeks. At this stage, the goal is to identify compounds which exhibit some activity.

The project team then analyzes these compounds to decide which of them is the most promising starting point for optimization using the art of medicinal chemistry. Obviously, huge amounts of data are generated, and powerful IT tools are required to extract the knowledge we need. To really understand the data, we visualize it and study the relationship between chemical structures and biological properties.

Target and compound fit together like a lock and a key. The compound can be modified so that it fits better and, ideally, becomes more potent. Medicinal chemistry involves the

use of chemistry's tools to design molecules that are potential drugs. We manipulate the molecular structure and then send the compounds back to our biologists or pharmacologists for testing in an iterative process. With each cycle, the compound is further optimized to finally become a drug.

At first, we seek to enhance the potency of the compound's effects on the target protein, but as we advance we look at other activities, which may cause side effects. The aim is to ensure that the compound's overall properties allow it to become a drug. For example, our electrophysiologists screen drugs for side effects by monitoring electrical activity in the heart or brain. Here, electrical communication depends on ion channels in the cell membrane; if a drug blocks some of these ion channels, it can have serious adverse effects.

Small-scale testing for initial assays requires only milligram quantities; for subsequent testing, however, much more material is needed. This is where our process research teams come into the picture. They are responsible for scaling up from milligram to gram quantities, and finally to the kilogram batch which is used for preclinical testing.

It's no good having a potent compound which is destroyed by the body before it has a chance to do its job. Our chemical and drug product specialists take a compound which has been optimized by the chemists and develop the most robust, safe and cost-efficient processes for the drug substance, the formulation, and packaging materials.

Once reproducible processes have been elaborated to produce large quantities of the active compound and the formulated drug product, our technical project teams manage the production of the drug with partner companies. They secure drug supplies for clinical development and, when appropriate, for commercial launch and beyond.

Building the clinical evidence

Following the drug discovery phase, the selected molecule must be comprehensively studied to demonstrate clinical safety and efficacy.

Idorsia aims to deliver new products with the potential to significantly change the treatment options for the target diseases. We want to bring new perspectives to the development of innovative compounds, challenging accepted paradigms to answer the questions that matter most. Our key assets have the potential to transform treatment in the target indications.

Idorsia's clinical development function comprises a broad spectrum of expertise clustered within multiple departments: therapy area units, strategic development, clinical pharmacology, biostatistics and data management, drug safety, drug regulatory affairs, clinical operations and life cycle management. Life cycle cross-functional teams – under the direction of a life cycle leader – bring expertise from preclinical development, clinical development and

technical operations to the efficient development of new medicines. They steer the compounds from entry into human studies through to submission of the dossier to health authorities, approval and maintenance of the license during the commercialization phase up to the loss of the medicine's exclusivity in the major markets and beyond. Idorsia's clinical development function manages clinical programs in accordance with the appropriate ethical, scientific, medical and operational standards, so as to generate the information required by regulatory health authorities worldwide.

Regulatory review

With successful clinical studies demonstrating a compound's safety and efficacy in hand, we must then navigate the regulatory review and approval process. From the first-in-human study of a drug through market approval and for as long as it remains on the market, we maintain an ongoing dialogue with health authorities in every country where we operate. We ensure that our development plans meet the regulators' expectations and that we generate the types of data that are required to support registration of the product.

Once our products reach the registration phase, we embark on the regulatory review process. Teams from across Idorsia collaborate to develop a robust and comprehensive dossier for submission to the health authorities. The data included is wide reaching: preclinical research, such as compound screening, animal models and all pharmacology, pharmacokinetics and toxicology data; technical descriptions of the properties and chemical synthesis of the drug substance, as well as quality controls and procedures for pharmaceutical manufacturing; and complete results and analysis of each of the clinical studies and safety data collected over the course of clinical phases – in other words, the story of each molecule from bench to bedside.

Product launch and commercialization

Regulatory approval is a key milestone, but our treatments can only reach patients if our products are successfully launched by our commercial organization – completing the journey from bench to bedside.

Our approach to launch starts long before approval, with the global product strategy – a roadmap to accelerate our affiliates' efforts to successfully launch our products, while also providing a consistent foundation across the world.

Within our commercial organization, three functions – Marketing, Medical Affairs

and Value & Access – are responsible for the global product strategy, in close collaboration with key country leaders and our discovery and development teams.

Global Marketing generates deep insights from patients and healthcare professionals, which help us to gain a holistic understanding of our customers' needs. This helps us to address unmet needs in the marketplace and to clearly differentiate our brands. We also focus our marketing efforts on raising awareness among patients, healthcare professionals and other key stakeholders (e.g. policymakers) of the impact of the conditions targeted by our products.

Idorsia's Global Medical Affairs team is responsible for communicating to the healthcare community our science, the data on our products, and the key differences from other treatments. To inform and develop our global strategy, we also seek medical insights regarding how our products' core data resonates with physicians. Our medical and clinical development teams continue to generate new evidence for approved products – with real-world evidence in high demand among payors and physicians alike. Importantly, this team also manages Idorsia's repository of medical information and has developed an intelligent digital platform, providing 24/7 self-service access to scientifically robust, balanced, and easily digestible information.

Value & Access is responsible for demonstrating the value of our products – which is more important than ever, given increasing budgetary constraints in healthcare systems across the world. As an engaged member of the healthcare ecosystem, Idorsia understands its role as helping to find solutions to the high cost of healthcare, and we are committed to playing our part in supporting patient access to our medicines. The prices of our medicines will reflect the value that our innovations deliver, generating revenues to fuel the discovery and development of future molecules. To demonstrate meaningful innovation, we develop a value proposition, underpinned by our science and clinical data, to help payors determine the value offered by our treatments compared to existing options. Our ultimate goal is to help patients gain access to our treatments through reimbursement or other coverage arrangements.

While our product strategies are global, our country teams own the execution of their local launches and customer relationships, and they tailor the global strategies to their markets. Working closely together, our affiliates and global teams all play a role in ensuring a successful launch and thus maximizing the value of Idorsia's innovation.

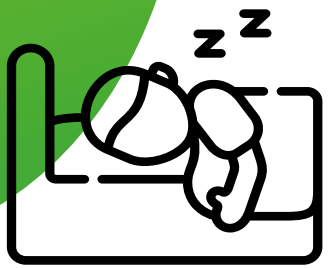
Our innovative products

PIVLAZ® (clazosentan) 150 mg, a selective endothelin A (ETA) receptor antagonist, has been approved by the Japanese health authorities (PMDA) for the prevention of cerebral vasospasm, vasospasm related cerebral infarction and cerebral ischemic symptoms after aneurysmal subarachnoid hemorrhage (aSAH).

Aneurysmal subarachnoid hemorrhage (aSAH) involves sudden life-threatening bleeding occurring in the subarachnoid space. It is caused by the rupture of an aneurysm – a weak, bulging spot on the wall of a cerebral artery. An emergency procedure (endovascular coiling or microsurgical clipping) is required to secure the aneurysm to prevent rebleeding. The incidence of aSAH is particularly high in Japan with approximately 22.5 cases per 100,000 person-years.

Bleeding and the release of endothelin-1 – a potent vasoconstrictor produced mainly by the neighboring vascular endothelium – can lead to cerebral vasospasm (constriction of arteries in the brain), which usually starts 3 days after aSAH onset and peaks in intensity between 8 and 11 days. This diminishes blood flow to the brain, and about one third of all aSAH patients consequently experience worsening of their neurological condition. Cerebral vasospasm is one of the leading secondary causes of disability in patients with aSAH.

Until now, physicians have had limited treatment options to prevent cerebral vasospasm, vasospasm related cerebral infarction and cerebral ischemic symptoms after aSAH, and PIVLAZ is considered to be the first innovation in aSAH treatment in Japan in over 25 years.



QUVIVIQ™ (daridorexant) is approved in the US, EU and the UK for the treatment of adult patients with insomnia. Insomnia is a condition of overactive brain activity during sleep, and studies have shown that areas of the brain associated with wakefulness remain more active during sleep in patients with insomnia.

Poor-quality or insufficient sleep can affect many aspects of the daily lives of people with trouble sleeping, including the ability to concentrate, mood and energy levels. In the long term, insomnia is associated with numerous serious health conditions, such as psychiatric disorders, cardiovascular disease, substance abuse and dementia.

Rather than inducing sleep through broad inhibition of brain activity, QUVIVIQ blocks only the activation of orexin receptors. Consequently, QUVIVIQ decreases the wake drive, allowing sleep to occur, without altering the proportions of sleep stages.

QUVIVIQ is a dual orexin receptor antagonist (DORA), which blocks the binding of the wake-promoting neuropeptides orexins and is thought to turn down overactive wakefulness in insomnia. QUVIVIQ is the first and only DORA approved in the European Union.

Our innovation pipeline

We have a diversified and balanced clinical development pipeline that covers multiple therapeutic areas, including CNS, cardiovascular and immunological disorders, as well as orphan diseases.

We report regularly with updates on our innovation pipeline as part of our quarterly financial results.

Visit our website to review our
Innovation Pipeline

Partnerships

We believe that collaboration is key to getting cutting-edge therapies to patients around the world in the most effective way possible. Partnerships form an integral part of our business and maximize the potential of innovation by providing strategic access to technologies or products and fully exploiting our discovery engine and clinical pipeline.

For further information on partnerships, see the **Partnerships info sheet.**

About this report

Company profile

Headquartered in Allschwil, Switzerland – a European biotech hub – Idorsia is a high-potential biopharmaceutical company, specialized in the discovery, development and commercialization of innovative small molecules, with the aim of transforming the horizon of therapeutic options. The company has an experienced team of over 1,300 highly qualified professionals covering all disciplines from bench to bedside, and commercial operations in Europe, Japan, and the US – the ideal constellation for bringing innovative medicines to patients.

We are committed to achieving our ambitious goals in an economically, socially and environmentally responsible manner, and, as the company grows, our commitment to sustainability remains as important as ever.

We have a diversified and balanced clinical development pipeline covering multiple therapeutic areas, including CNS, cardiovascular and immunological disorders, as well as orphan diseases. Two Idorsia products are commercially available – QUVIVIQ™ (daridorexant) in the US and Europe, and PIVLAZ® (clazosentan) in Japan.

Idorsia Ltd is the Group's holding and finance company, with 14 subsidiaries across Europe, Asia and the US. Idorsia was listed on the SIX Swiss Exchange (ticker symbol: IDIA) in June 2017.

About our sustainability reporting

The information contained in this info sheet covers the period from January 1, 2020 to December 31, 2022 and pertains to all significant locations of operation. In the context of its sustainability reporting, Idorsia considers significant locations of operation to be those with more than 20 permanent employees. Currently, this includes locations in Switzerland, the US and Japan. Any deviations from this reporting framework are indicated on a case-by-case basis.

The content of our sustainability reporting is aligned with the results of a materiality assessment and references the internationally recognized guidelines of the **Global Reporting Initiative (GRI).**

For the full set of ESG info sheets, visit
www.idorsia.com/sustainability