Research and Development

At Novartis, Research and Development work together seamlessly in an effort to bring new and better medicines to market in the shortest possible time.

This effort involves two phases: an “exploratory phase,” during which a candidate compound is discovered and a Proof of Concept (PoC) is established through studies in patients; and a “confirmatory phase,” during which the drug enters full development when studies in large numbers of patients are conducted.

In the first phase, scientists and physicians from the Novartis Institutes for BioMedical Research (NIBR) work in multi-disciplinary teams to move compounds along through initial tests in man.

The Development function then leads confirmatory testing and the process of gaining regulatory approval.

The exploratory phase: drug discovery

All drug discovery efforts at Novartis focus on patients. Scientists determine which diseases will be the focus of research efforts based on two questions: do we have, or can we gain, significant understanding of the cause, or mechanism, underlying the disease? And does this disease represent a significant unmet medical need? If the answer to both questions is yes, then Novartis develops a research program aimed at better understanding the disease and finding an effective therapy. Early-discovery science determines how a disease is caused at the molecular level, using our own discoveries as well as those from external collaborators. We look for clues in both patients’ experience of the disease and the compendium of historical medical and scientific knowledge, integrated with the growing knowledge of human biology, chemistry and genetics.

Target discovery and drug design

Typically, making a drug begins with identifying a protein associated with human disease. These proteins are known as “targets.” When it is confirmed that a target plays a role in a disease, an experiment known as a high-throughput screen is conducted to find a chemical compound or antibody that binds or “hits” the target in a way that alters the disease. Once chemical compounds or antibodies are identified by their binding to a target, these hits are enhanced to improve their safety and effectiveness. The resulting chemical compound or antibody becomes a drug candidate.

Preclinical safety and efficacy

An initial profile of a drug candidate’s safety and effectiveness must be determined before it is tested in humans. In this phase, scientists use computer models and laboratory tests to assess the safety of a drug candidate. These tests determine how well a drug candidate is absorbed, where it goes within the body,
how it is broken down or metabolized, and how quickly and in what manner it is eliminated from the system.

Proof of Concept and Phase I

In Proof-of-Concept (PoC) trials, the drug candidate is given to a small group of patients (five to 15) to determine how the target functions in the human body, or its “mechanism of action,” and to get an early understanding of how the drug candidate alters human disease. After a successful PoC trial, a drug candidate may enter Phase I trials (20-80 patients or healthy volunteers) to evaluate its safety, determine the safe dose and identify side effects. Sometimes drug candidates go directly from PoC to Phase II trials.

The confirmatory phase: drug development

Clinical development (Phases II and III)

In Phase II trials, the drug is given to a larger group of patients (100-300) to test its effectiveness, determine the appropriate dose, and to further evaluate its safety. In Phase III trials, the drug is given to large groups of patients (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used existing treatments and collect information that will allow the medicine to be used safely.

Registration/post-launch

To register a new drug, the results of all preclinical and clinical studies, along with the description of the manufacturing process, are compiled and submitted to regulatory authorities. If regulators agree that the data establish the quality, efficacy and safety of the drug, a marketing authorization is granted. The new drug can then be made commercially available to patients. Once a drug is on the market, adverse effects need to be constantly monitored and reported to regulatory authorities. In addition, life-cycle programs – including Phase IV clinical trials – are often undertaken to explore and add new indications or improve existing formulations of the drug.

Pharmaceuticals

We are a leader in the pharmaceuticals industry in terms of research and development, including the level of our investment. Our Pharmaceuticals Division expensed USD 7.3 billion (on a core basis USD 7 billion) in research and development in 2014. This represented 23% (on a core basis 22%) of the division's total net sales.

Novartis Institutes for BioMedical Research (NIBR)

The Novartis Institutes for BioMedical Research (NIBR) is the global pharmaceutical research organization of Novartis. With more than 6,000 scientists, physicians and business professionals around the world, NIBR focuses on discovering innovative new drugs that can change the practice of medicine.
A truly global research network

The continued commitment of Novartis to pharmaceutical research and development has resulted in a robust pipeline and a strong track record of bringing innovative medicines to market. With an ongoing focus on diseases for which medical needs remain unmet, scientists and physicians at NIBR are dedicated to ensuring that Novartis maintains its strong pipeline.

Headquartered in the United States in Cambridge, Massachusetts, the NIBR research network includes a major research center in Basel, Switzerland, and additional centers in East Hanover, New Jersey; Emeryville and San Diego, California USA; and Shanghai, China.

Commitment to diseases of the developing world

Research for diseases of the developing world is ongoing throughout NIBR’s global network of research sites. In addition, an institute within NIBR, the Novartis Institute for Tropical Diseases (NITD) in Singapore is fully dedicated to discovering treatments for neglected diseases.

The Novartis Institute for Tropical Diseases (NITD)

The Novartis Institute for Tropical Diseases focuses on discovering novel treatments and prevention methods for major tropical diseases. In developing countries where these diseases are endemic, Novartis intends to make treatments readily available to poor patients without profit. The discovery technology at NITD is state-of-the-art, and the scope of activities includes target discovery, screen development, compound optimization, preclinical development and Proof-of-Concept clinical trials. NITD also offers teaching and training opportunities for postdoctoral fellows and graduate students.

The NITD research projects focus on several tropical diseases including dengue and malaria.

Alcon

In 2014, our Alcon Division expensed USD 0.9 billion (on a core basis USD 0.9 billion) in research and development, which amounted to 9% of the Division’s net sales.

Our Alcon Division associates in research and development work to address diseases and conditions that affect vision, such as cataracts, glaucoma, retina diseases, dry eye, infection, ocular allergies and refractive error. Our Alcon Division invests approximately USD 1 billion annually to drive research and new product development in eye care. Alcon's pipeline strategy is built around a proof-of-concept qualification process, which quickly identifies opportunities that have the best chance for technical success and advances those projects, while terminating others with a low probability of success.

For Alcon’s Ophthalmic Pharmaceuticals franchise, NIBR engages in research activities in an effort to discover and expand ophthalmic targets, and to develop
chemical and biologic compounds for the potential treatment of diseases of the eye, with a particular focus on diseases such as glaucoma and macular degeneration. The costs for these activities are allocated to Alcon.

Research and development activities for Alcon’s Surgical franchise are focused on expanding intraocular lens capabilities to improve refractive outcomes and on developing instruments for cataract, vitreoretinal and corneal refractive surgeries. The focus for the Vision Care franchise is on the research and development of new lens materials, coatings and designs to improve patient comfort, and on lens care solutions that provide the safety, disinfecting and cleaning power needed to help maintain ocular health. As announced in 2014, Alcon is also collaborating with Google[gm], and has licensed its smart lens technology for ocular medical uses, including the potential to monitor glucose levels in diabetic patients and provide an accommodative contact lens/intraocular lens for patients living with presbyopia. The Ophthalmic Pharmaceuticals franchise is focused on the development of products for the treatment of retinal diseases, glaucoma (intraocular pressure lowering) and ocular allergy.

Sandoz

Before a generic pharmaceutical may be marketed, intensive technical and clinical development work must be performed to demonstrate, in bioavailability studies, the bioequivalency of the generic product to the reference product. Nevertheless, research and development costs associated with generic pharmaceuticals generally are much lower than those of the originator pharmaceuticals, as no pre-clinical studies or clinical trials on dose finding, safety and efficacy must be performed by the generic company. As a result, pharmaceutical products for which the patent and data exclusivity period has expired can be offered for sale at prices often much lower than those of products protected by patents and data exclusivity, which must recoup substantial basic research and development costs through higher prices over the life of the product's patent and data exclusivity period.

While generic pharmaceuticals are follow-on versions of chemically synthesized molecules, so-called “biosimilar” products contain a version of the active substance of an already approved original biological medicine. Due to the inherent variability of biologic products and their higher complexity, the development and the regulatory pathway of biosimilars differ significantly from that of generics.

Development of a biosimilar product is much more technically challenging than the development of a generic pharmaceutical. Unlike generic pharmaceuticals, development of biosimilars requires clinical studies in patients. Biosimilars are engineered to match the reference product in quality, safety and efficacy. This is achieved by systematically defining the target of the reference product and then comparing the biosimilar to the reference product at various development stages to confirm biosimilarity and to establish that there are no clinically meaningful differences between the proposed biosimilar and the reference biologic. Because the purpose of a biosimilar clinical development program is to confirm biosimilarity and not establish efficacy and safety de novo, the clinical studies required are less than those required for an originator biologic, and no pre-clinical studies are
required. Therefore, the cost of development for a biosimilar is usually less than that of an originator biologic.

The regulatory pathways for approval of biosimilar products are being developed and established in many countries of the world. A regulatory framework for the approval of biosimilars has been established in the EU, Japan, Canada and US, while the WHO issued guidance. Sandoz has successfully registered and launched the first biosimilar (or biosimilar type) product in Europe, the US, Canada, Japan, Taiwan, Australia and many countries in Latin American and Asia. Sandoz has three approved biosimilar products in more than 60 countries of the world, and is the first company to file a Biologics License Application (BLA) for marketing approval of a biosimilar in the US.

Currently, the affiliates of the Sandoz Division employ more than 2,700 Development and Registration staff who explore alternative routes for the manufacture of known compounds and develop innovative dosage forms of well-established medicines. These associates are based worldwide, including facilities in Holzkirchen and Rudolstadt, Germany; Kundl, Schaftennau and Unterach, Austria; Ljubljana and Mengeš, Slovenia; Boucherville, Canada; and East Hanover, New Jersey. In 2014, Sandoz expensed USD 0.8 billion (on a core basis USD 0.8 billion) in product development, which amounted to 8% of the division’s net sales.
Disclaimer

These materials contain forward-looking statements that can be identified by words such as “potential,” “expected,” “will,” “planned,” or similar terms, or by express or implied discussions regarding potential new products, potential new indications for existing products, or regarding potential future revenues from any such products; regarding potential shareholder returns or credit ratings; regarding the potential completion of the announced transaction with CSL; regarding the potential financial or other impact on Novartis of the transactions with GSK, Lilly or CSL; or regarding any potential strategic benefits, synergies or opportunities as a result of these transactions; or regarding potential future sales or earnings of the Novartis Group or its divisions and associated companies; or by discussions of strategy, plans, expectations or intentions. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that any new products will be approved for sale in any market, or that any new indications will be approved for any existing products in any market, or that any approvals which are obtained will be obtained at any particular time, or that any such products will achieve any particular revenue levels. Nor can there be any guarantee that the announced transaction with CSL will be completed in the expected form or within the expected time frame or at all. Neither can there be any guarantee that Novartis will be able to realize any of the potential strategic benefits, synergies or opportunities as a result of the transactions with GSK, Lilly or CSL. Neither can there be any guarantee that the Novartis Group, or any of its divisions or associated companies, will be commercially successful in the future, will achieve any particular financial results, or achieve any particular credit rating or level of shareholder returns. Nor can there be any guarantee that the turnaround plan under development at Alcon will be successfully developed or implemented, or will achieve its goals. In particular, management’s expectations could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally, including an unexpected failure to obtain necessary government approvals for the announced transaction with CSL, or unexpected delays in obtaining such approvals; the potential that the strategic benefits, synergies or opportunities expected from the transactions with GSK, Lilly or CSL may not be realized or may take longer to realize than expected; the inherent uncertainties involved in predicting shareholder returns or credit ratings; the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; the Company’s ability to obtain or maintain proprietary intellectual property protection, including the ultimate extent of the impact on the Company of the loss of patent protection and exclusivity on key products which will continue this year; unexpected manufacturing or quality issues; unexpected safety issues; global trends toward health care cost containment, including ongoing pricing pressures and ongoing reimbursement challenges with payors; uncertainties regarding actual or potential legal proceedings, including, among others, actual or potential product liability litigation, litigation and investigations regarding sales and marketing practices, government investigations and intellectual property disputes; general economic and industry conditions, including uncertainties regarding the effects of the persistently weak economic and financial environment in many countries; uncertainties regarding future global exchange rates; uncertainties regarding future demand for our products; uncertainties involved in the development of new healthcare products; uncertainties regarding potential significant breaches of data security or disruptions of the Company’s information technology systems; and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in these materials as of this date and does not undertake any obligation to update any forward-looking statements as a result of new information, future events or otherwise.