Jennifer Allport-Anderson sees life dramas reflected in the cells she studies.

Research and development

Better treatments for neglected diseases are a crucial priority to achieve our vision of equitable global health. For some diseases, current therapies are encountering increasing resistance, while for others, existing drugs have unacceptable side effects or no drugs are available at all. In recent years, there has been a much-welcomed boost in R&D for neglected diseases, catalyzed by partnerships between academia, pharmaceutical companies, charities and governments. However, we need all sectors to step up investment and increase their efforts to ensure these treatments reach the patients in need.”

Trevor Mundel, President of the Global Health Division at the Bill & Melinda Gates Foundation

Why it is important

Research and development as well as a strong pipeline of potential medicines are critical for future business and long-term success. R&D remains a cornerstone of the Novartis strategy and a foundation of our future. We invested USD 9.0 billion on R&D for new drugs and medical devices in 2016, or 18.6% of net sales. Our teams made progress toward fighting devastating diseases ranging from breast cancer to multiple sclerosis to malaria.

We believe innovation that produces breakthrough medicines, devices and solutions will be critical in the coming years as demographic trends increase pressure on healthcare systems to produce the best results at the lowest overall cost. Innovation more broadly is also a key enabler of access to healthcare. Altogether, this supports our efforts to grow in emerging markets and can help us respond to unmet medical needs of patients, whether in the developed or developing world.

How we approach it

Our R&D strategy sets clear priorities. We concentrate on therapeutic areas where there is patient need and where scientific advances present new opportunities, including oncology, cardiovascular, eye care, biosimilars and neuroscience.

We are also exploring new scientific frontiers in areas with great potential for innovation, including immunology, aging and regenerative medicine, and infectious diseases.

We seek to develop medicines and products that can generate positive real-world outcomes for patients and healthcare providers. The benefits can range from improving the cost-effectiveness of high-quality care to prolonging lives. We are developing services and technologies to increase the benefits of our core products, often in collaboration with healthcare providers and technology companies.
To focus our resources, we completed a portfolio prioritization exercise for projects in development, which led to the acceleration of certain projects and the termination of others. We are concentrating on therapies we believe have the greatest potential to change the practice of medicine, with more than 200 projects in clinical development.

The Novartis Institutes for BioMedical Research (NIBR) is the innovation engine of Novartis. In 2016, we updated our research strategy to ensure that we remain a discovery powerhouse. We are increasing collaboration across traditional scientific and organizational boundaries, with a focus on powerful new technologies that have the potential to help produce therapeutic breakthroughs.

Drug development

When molecules are ready for testing in humans, we organize proof-of-concept studies enrolling small numbers of patients to make an early assessment of a drug’s safety and effectiveness.

After a successful proof-of-concept study, our development team decides whether to begin larger clinical trials to test effectiveness and safety in additional patients. We pursue therapies where we can leverage the scale and expertise of Novartis development operations to bring important treatments to large numbers of patients.

In 2016, we created a single Global Drug Development group to manage clinical development for all our therapeutic areas, advancing molecules ranging from checkpoint inhibitors for cancer to a peptide for heart failure to biosimilars for a variety of diseases. This work was previously conducted individually by several organizations within the company. By integrating our development organization, we aim to leverage our collective strength. We can now look at our entire mid-stage pipeline across our Innovative Medicines and Sandoz businesses to identify projects that hold the most promise and take steps to ensure they are properly resourced.

More information on R&D can be found in the innovation section, pages 40-57, of the Novartis Annual Report 2016, and on our website.

How we perform

Infectious diseases

Bacteria, viruses and other micro-organisms continue to significantly impact human health, despite major medical advances. Infectious diseases remain the leading cause of death in children and adolescents, and one of the leading causes of death in adults. We are working across the spectrum of these diseases, including tropical diseases such as malaria that alone kills almost 430,000 people each year.

The Novartis Institute for Tropical Diseases (NITD) is dedicated to finding new medicines for malaria, dengue fever, human African trypanosomiasis and other neglected diseases. In October, we announced that NITD will move its operations and research programs from Singapore to Emeryville, California in the US, where it will be co-located with the infectious diseases research team of NIBR. This move will strengthen NITD for the future by enabling closer collaboration with the NIBR infectious diseases research team and the San Francisco Bay Area life sciences community.

Drug-resistant parasites are spreading in certain regions, so new drugs are urgently needed. Through NITD, we have two compounds in Phase II development for malaria: KAF156 and KAE609.

In September, the results of a proof-of-concept study for KAF156 were published. Malaria parasites, including parasites resistant to the standard treatment, were observed to disappear rapidly from the blood of patients who received either multiple or single doses of the compound in an exploratory Phase II clinical trial. We will lead the development of KAF156 with scientific and financial support from the Medicines for Malaria Venture (in collaboration with the Bill & Melinda Gates Foundation). We are exploring ways to combine it with another agent to develop a new treatment option for malaria that is active against drug-resistant parasites, and it could potentially become a single-dose malaria cure. KAE609 continues to be evaluated for the role that it may play in the battle against the disease.

Scientists are obsessed with the differences between academia and industry, and I just don’t see it anymore. The culture of science at the basal level is just this hope of being connected to a great idea and then seeing it through to completion. In this moment, pharmaceutical companies are much more interested in public-private partnerships, in open modes of discovery, than ever before. I think this is an evident trend in the industry, and we are well poised at Novartis to be a trendsetter and exemplary leader. In my opinion, connectivity is the new scientific priority.”

Jay Bradner, M.D., President, Novartis Institutes for BioMedical Research
We also reported a new target for three neglected diseases: African sleeping sickness, leishmaniasis and Chagas disease. Clinically, these diseases – responsible for 50,000 deaths annually – seem quite distinct, but they are all caused by parasites called kinetoplastids that belong to the same class of single-celled organisms. Working in lab models, our researchers demonstrated that it may be possible to treat all three diseases with a single class of compound that blocks cellular machinery known as the proteasome.

Novartis has a long history in developing antibiotic treatments, and we continue to conduct research into new antibiotic treatments for the most devastating infectious diseases. In 2016, we began a first-in-human clinical trial to test an injectable compound designed to kill drug-resistant gram-negative bacteria.

About 66 million patients take our medicines to tackle bacterial infections every year, and we are working to broaden access to these treatments in underserved markets around the world. Our generic medicines division, Sandoz, is also the world’s largest generic antimicrobial producer.

High-quality generic anti-infective medicines are a key part of the provision of global healthcare, underpinning most common surgical procedures and treatments such as chemotherapy, as well as treating acute bacterial infections. More than 70% of anti-infectives sold globally are generic medicines.

Adaptive R&D is the modification of an existing medicine to improve therapeutic efficacy, safety, and access to medicine, and – most importantly – to generate a positive health outcome. Most often, this work is done with a specific focus on poor and vulnerable patient groups, such as children or the elderly.

Our Established Medicines franchise manages a product portfolio of more than 90 mature brands that span 11 therapeutic areas. We systematically evaluate and execute adaptive R&D projects related to mature products in our existing portfolio.

These may include development of new formulations that deliver an incremental benefit to patients, such as age-appropriate formulations, formulations that increase adherence, or dosage forms with increased stability and new routes of delivery. As an example, we are currently working on developing a once-daily form for lumefantrine, which is also a key component of Coartem, our artemisinin-based combination therapy against malaria.

We also look for ways to expand the clinical use of existing medicines into new indications and populations. This includes ongoing work on new indications, such as multidrug-resistant tuberculosis for Lamprene (clofazimine), an agent to treat leprosy.

In addition, our Center of Excellence for Emerging Markets collaborates closely with the global program teams across the Innovative Medicines Division to ensure that adaptive R&D considerations, especially formulations for specific age groups or geographies, are firmly embedded in the development plans for our new products.

Fighting antimicrobial resistance
Drug-resistant bacteria are an emerging threat to public health. In 2016, we joined with leading industry peers to present a roadmap for combating antimicrobial resistance (AMR). The signatories made four key commitments they will deliver by 2020 to reduce AMR: reduce the environmental impact of the production of antibiotics; help ensure antibiotics are used only by patients who need them; improve access to current and future antibiotics, vaccines and diagnostics; and explore new opportunities for open collaboration between industry and the public sector.

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Scientific capability building
We contribute to building scientific and clinical capabilities in emerging countries through the Novartis Next Generation Scientist and Visiting Scholar programs. Since 2010, 165 young scientists and clinicians from 24 countries across Africa, Asia and Latin America have participated in these programs.

Additionally, since 2011, the WHO Tropical Disease Research (TDR) group has sponsored clinical research fellows at Novartis. NIBR has also been participating since 2014 in a fellowship scheme set up by the European & Developing Countries Clinical Trials Partnership (EDCTP) together with the European Federation of Pharmaceutical Industries and Associations (EFPIA). The primary objective of the EDCTP-EFPIA and WHO TDR programs is to support capacity-building efforts by providing opportunities for sub-Saharan African scientists to gain hands-on clinical trial experience in a pharmaceutical research setting. In 2016, a scientist from Addis Ababa University in Ethiopia started a one-year fellowship at NIBR.

In 2016, we also assisted clinical research centers in Kenya, Ghana, South Africa and Tanzania in strengthening their capabilities to conduct and manage Phase I clinical trials. This was achieved through a multifaceted approach involving scientific exchange, infrastructure development, and educational programs.
# Innovation key performance indicators

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<thead>
<tr>
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<th>2016</th>
<th>2015</th>
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<tbody>
<tr>
<td>Projects entering development pipeline</td>
<td>5</td>
<td>8</td>
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<tr>
<td>Ongoing Phase III programs</td>
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<td>37</td>
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<tr>
<td>US FDA breakthrough therapy designations</td>
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<td>Major submissions (US, EU, JPM)</td>
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<tr>
<td>Major approvals (US, EU, JPM)</td>
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<td>New molecular entity (NME) approvals</td>
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<td>6</td>
</tr>
<tr>
<td>Investment in infectious and neglected diseases</td>
<td>29</td>
<td>42</td>
</tr>
</tbody>
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1. Includes Innovative Medicines and Sandoz biosimilars only
2. Includes programs entering confirmatory development, based on internal R&D activities. First patient, first visit (FPFV) has occurred in post-proof-of-concept stage. Also includes small molecules, biologics, new fixed-dose combinations of existing active pharmaceutical ingredients (APIs), and new target indications, defined as new disease or new line of treatment (e.g., first line vs. second line). Counted by indication and not compound.
3. This number has been adjusted due to the revised definition of projects entering portfolio. In 2015, we reported it as 25.
4. Includes projects with FPFV in a Phase III study but not yet filed in the US, EU or Japan.
5. Number of breakthrough therapy designations by the US Food and Drug Administration for therapies under development by Novartis.
6. Includes small molecules, biologics, new fixed-dose combinations of existing APIs; and new target indications, defined as new disease or new line of treatment (e.g., first line vs. second line).
7. Includes NMEs such as small molecules, biologics; in the EU, new fixed-dose combinations of existing APIs.
8. USD millions.
9. Novartis Institute for Tropical Diseases and Novartis Institutes for BioMedical Research neglected disease programs, and pharmaceutical development on malaria, tuberculosis and neglected diseases.

Targets and commitments can be found on our website.