Delivering on the promise of cell and gene therapy for patients

Patients with the most common childhood cancer, acute lymphoblastic leukemia (ALL), often battle the disease for years. Life for these brave kids—who undergo round after round of chemotherapy in an effort to keep their disease in check—is anything but normal. They are in and out of the hospital and must deal with the side effects of chemotherapy, including fatigue and nausea. If their cancer doesn’t respond to the standard treatments, then an unjust, premature death becomes a certainty. At least until recently.

New advances in cell and gene therapies offer the potential to transform medicine. They create an inflection point in our ability to treat—and even potentially cure—many intractable illnesses.
At Novartis, we’ve been pioneers on the cell and gene therapy frontier. Working with emerging tools, we are pushing at the edge of what is possible to bring entirely new types of treatments to patients with devastating diseases, including genetic disorders and certain deadly cancers. We’re reimagining medicine to produce breakthroughs and address major unmet needs.

Cell and gene therapies are designed to halt a disease in its tracks or reverse its progress rather than simply manage symptoms. They are often one-time treatments that may alleviate the underlying cause of a disease and they have the potential to cure certain conditions. In contrast, many conventional medicines must be taken continually for weeks, months, or even for life.

Cell and gene therapies are grounded in careful research that builds on decades of scientific progress. The underlying tools and technologies have been tested and refined by countless experts, first in the lab and later in the clinic with patients. With cell therapy, cells are
cultivated or modified outside the body before being injected into the patient, where they become a “living drug.” With gene therapy, genes are replaced, inactivated or introduced into cells—either outside or inside the body—to treat a disease. Some treatments such as Kymriah® qualify as both cell and gene therapy.

Kymriah® is a breakthrough therapy with the ability to reprogram a patient’s own immune cells to recognize and fight B-cell ALL. The reprogrammed immune cells are returned to the patient in a one-time infusion and are ready to begin detecting and destroying cancer cells, with many children achieving an early and lasting remission. Initially, children who receive the one-time treatment often experience serious side effects, which are frequently severe enough to require hospitalization. While not all patients have a positive outcome, the majority of patients then begin to feel healthy and energetic. It will be decades before anyone can claim with certainty that these kids are cured, but some of the first patients to receive the one-time treatment have shown no signs of relapse for more than five years.

**Innovation in action**

This is a pivotal time for innovation in the field. Following key approvals of cell and gene therapies by health authorities, new treatments are being tested in clinical trials around the world. Novartis is leading the way, with a consistent history of working and investing to drive forward the research and development of such therapies. Kymriah®—the first gene therapy approved in the US—was the culmination of a multi-year collaboration with the University of Pennsylvania. It employs chimeric antigen receptor T-cell (CAR-T) technology. The team is now working to bring Kymriah® to patients in additional countries—including in the EU, where it’s been approved—as well as designing and testing new CAR-T therapies for a variety of difficult-to-treat cancers.

We are also developing cell and gene therapies to address genetic conditions, especially diseases caused by the mutation of a single gene. Initially, Novartis is focusing on conditions of the central nervous system, the eye and the blood because we have deep expertise in these areas and because it’s currently possible to deliver genetic material to these locations. In other words, we can get the cell or gene therapy to the relevant tissue. Novartis teams may expand into additional therapeutic areas in the future.

Our most advanced Neuroscience program is a gene therapy in clinical testing for spinal muscular atrophy (SMA), a rare disease caused by a defective or missing \( SMN1 \) gene. Health authorities in the US, EU and Japan have fast-tracked our application for the approval of this treatment for SMA Type 1. Without a functional \( SMN1 \) gene, infants with SMA Type 1 rapidly lose the motor neurons responsible for muscle functions such as breathing, swallowing, speaking and walking. Left untreated, a baby’s muscles become progressively weaker, eventually leading to paralysis or death, in most cases by his or her second birthday.
Delivered as a single, one-time infusion, our breakthrough treatment works by replacing the missing or defective SMN1 gene with a functional copy that makes SMN protein, thereby improving motor neuron function and survival. It was designed by scientists at AveXis and Nationwide Children’s Hospital. Novartis recently acquired AveXis to continue developing the treatment, as well as to explore additional applications for the underlying technology, a powerful gene therapy platform that may be relevant to other devastating diseases such as Rett syndrome and a genetic form of amyotrophic lateral sclerosis (ALS).

Novartis programs in ophthalmology and hematology are also focused on transforming patient care. For example, we recently acquired global rights outside the US to Luxturna®, a gene therapy designed by Spark Therapeutics to restore sight in children and adults with a rare, progressive genetic condition that leads to total blindness. Luxturna® was approved in the EU in November 2018 for the treatment of patients with vision loss due to a genetic mutation in both copies of the RPE65 gene. Patients must also have enough viable retinal cells to receive the therapy. Novartis collaborated closely with Spark on this milestone approval of the first gene therapy to treat an inherited retinal disease. We believe we have the expertise, scale and commitment to successfully commercialize such novel treatments in a variety of regions. We’re exploring innovative approaches to provide access for patients.

Collaborating on a frontier

While we are reimagining medicine, current healthcare systems are designed to actively manage chronic conditions, where treatment and therapies occur on a regular basis, sometimes over many years. They are not set up for therapies that provide a lifetime of benefit following a single infusion. One-time cell and gene therapies introduce a number of unprecedented complexities in diagnosis, treatment, care and payment. We are collaborating with governments, hospitals, doctors and payers to support rapid diagnosis and the use of cell and gene therapies, when they are appropriate.

All of these efforts complement our conventional drug discovery and development programs. We continue to work with small molecules and biological molecules, which are therapeutic staples. When it’s clear, however, that these tools won’t work, we don’t give up. Instead we hunt for new ways to treat diseases, including by exploring cell and gene therapies.

Novartis has made one of the largest investments in cell and gene therapy in the industry. We are building on the momentum of recent approvals from health authorities, with more than a dozen projects in clinical development and additional research underway. We believe in the promise of these exciting new medicines and will continue to work to advance them for patients.

Work with us
To learn about opportunities to join our team, visit our Careers section.

Footnotes:

1. Kymriah® is approved in the US and EU for patients with B-cell ALL that is refractory (the disease did not go into remission with other leukemia treatments) or in second or greater relapse (the disease went into remission and then came back). Kymriah® is also approved in the US and EU for a particular type of relapsed or refractory large B-cell lymphoma in adult patients.

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