

Innovation in the Biopharmaceutical Pipeline

The Promise of the Pipeline



The biopharmaceutical pipeline contains thousands of potential new treatments providing hope to patients by addressing unmet medical needs, saving lives and improving patients' health. A new report by the Analysis Group, "Innovative Therapies and Vaccines in Clinical Development," examines the state of the drug development pipeline and provides insights into new approaches researchers are pursuing.

The research and development (R&D) process that leads to new treatments and potential cures for patients is lengthy, challenging and subject to substantial scientific and regulatory uncertainty. In fact, only 12% of investigational new medicines entering the clinical trial phase are ultimately approved by the U.S. Food and Drug Administration (FDA). **Our nation's innovative biopharmaceutical companies invest over \$91 billion¹ a year to harness new scientific and technological advances to bring new medical advances forward**, such as treatments and vaccines for COVID-19, treatments for Hepatitis C, HIV, cancer, cystic fibrosis and neurodegenerative diseases.

Today, innovative medicines are saving and improving the lives of millions of Americans. New medicines have a significant impact on the U.S. health care system in terms of avoided hospitalizations, surgeries and other health care costs. Beyond improving patients' lives, the R&D investment by innovative biopharmaceutical companies contribute to the U.S. economy by supporting more than 4 million jobs across sectors.

Despite high costs and significant scientific and regulatory uncertainties, researchers continue to investigate new treatments across disease states, thanks in large part to the ongoing commitment of dedicated scientists and researchers and the substantial investments from the biopharmaceutical industry. In the last decade, biopharmaceutical companies have invested over half a trillion dollars in R&D and over 600 new medicines have been approved by FDA in the last decade.

Key findings from the report include:

- Nearly **70% of medicines** in clinical development are potentially first-in-class medicines, meaning they use different mechanisms of action from any other approved medicines.
- **About 1,135 projects** in clinical development received orphan drug designation by the FDA, which are critically important given **less than 10% of rare diseases²** have an approved medicine.
- **A range of novel scientific approaches** are being pursued, including cell and gene therapies, DNA and RNA therapeutics and conjugated monoclonal antibodies.

Potential First-In-Class

A first-in-class medicine is one that uses a different mechanism of action from any other already approved medicine. Such medicines offer new treatment options for patients, particularly for those who have not responded to existing therapies or for whom no treatment options are available. These medicines may improve the outlook for patients by providing greater efficacy, improved delivery or fewer side effects.

Across the entire clinical development pipeline 69% of projects are potentially first-in-class. When early-stage research projects, meaning research prior to in-human trials, are included, the number rises to almost 80% (77%) of projects as potentially first in class. High numbers of potential first-in-class medicines are seen in all phases of clinical development, but the percentage decreases for later stages in part because medicines with new mechanisms are less likely to make it through the development process due to higher levels of uncertainty.

Share of Potential First In Class Medicines For Selected Therapeutic Area Pipelines

80% Cardiovascular disease	72% Diabetes
75% Psychiatry	76% Neurology
93% Alzheimer's disease	68% Cancer

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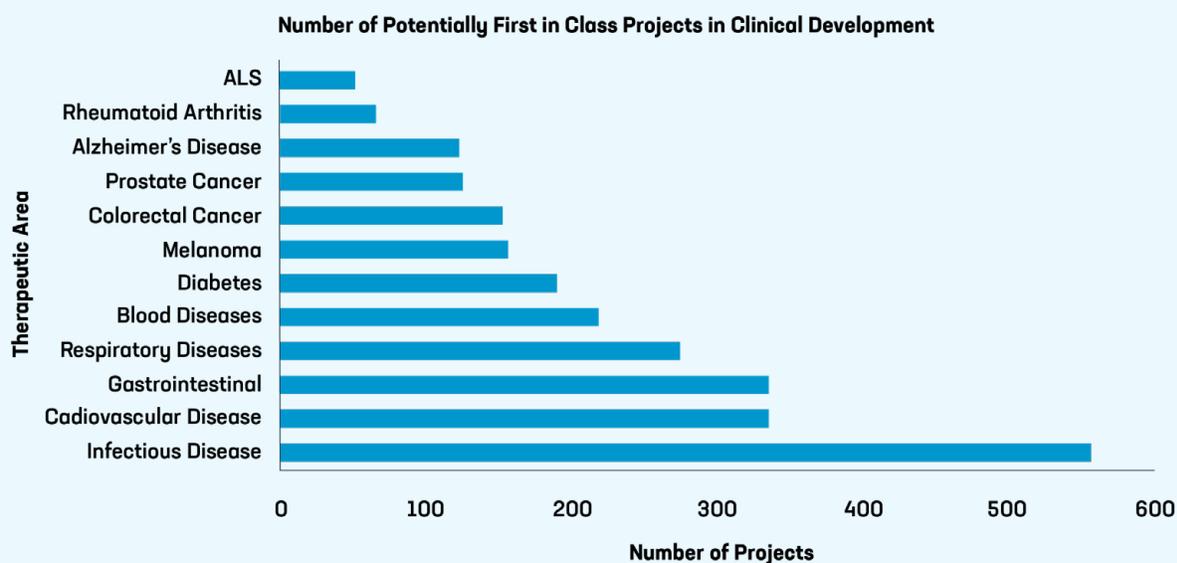
- **Blood cancers:** a first of its kind “off the shelf” cell therapy to target and kill cancer cells in the blood – involves the personalized modification of cells from healthy donors – uses innovative technology and streamlined manufacturing to allow the infusion into a cancer patient to happen in the outpatient setting.³
- **ALS:** a new mRNA treatment for ALS to reduce the production of the mutated protein that causes the fatal progression of ALS.⁴
- **Parkinson's Disease:** a single dose disease-modifying gene therapy delivers a nonmutated version of the gene that causes the inflammation and neurodegeneration, to the brain.⁵
- **HIV:** A potential first-in-class long-acting injectable antiviral treatment delivered once every 6 months for HIV infections not only offers significant convenience over once-daily dosing but tremendous hope to patients who may be resistant to multiple other classes of HIV drugs.⁶

Orphan Drug Projects For Selected Therapeutic Areas

520 Cancer	27 Cardiovascular
67 Immunology	40 Infections
40 Musculoskeletal	91 Neurology

*note: Figures represent Phase I, II, III and filed

SELECTION OF POTENTIAL FIRST IN CLASS MEDICINES BY THERAPEUTIC AREA



Treating Rare Diseases and Conditions

According to the National Institutes of Health (NIH), there are roughly 7,000 rare diseases, which, together, affect approximately 30 million people in the U.S. Among these diseases, over 90% have no approved medicines and more than 85% are serious or life threatening and 80% are genetic in origin. Medicines intended to treat these rare diseases affecting fewer than 200,000 people can be designated as orphan drugs.

The report found 1,135 products covered by an orphan designative were in active clinical development or regulatory review. The number of orphan designations has consistently grown over the past 30 years as scientific advances have allowed researchers to identify rare diseases more precisely. Qualifying for an orphan drug designation does not necessarily mean the project will ultimately be approved as an orphan drug as the investigational medicine must meet FDA's orphan drug criteria and approval standards. Orphan drugs are being developed across several disease states, including cardiovascular, cancer and neurology.



Across multiple fields of science, we stand at an inflection point in medicine – where new technology is creating foundational opportunities to treat and cure disease in ways that weren't possible just a short time ago... Over the next several years, we'll see this approach become a mainstay of treating, and probably curing, a lot of our most devastating and intractable illness.

Scott Gottlieb, MD, Former Commissioner, US Food and Drug Administration

Snapshot of Innovative Approaches to Fight Disease

New scientific discoveries are creating greater hope for the development of treatments for some of the most challenging diseases impacting patients. Molecular and biological targets that were beyond reach or completely unknown are becoming accessible with breakthroughs in basic science. The following platforms highlight a few innovative strategies that scientific researchers are using to fight disease:

- 545 **cell therapy** projects use the infusion or transplantation of whole cells into a patient's body to grow, replace or repair damaged tissue to treat a disease.
- 281 **gene therapy** projects that use genetic material to manipulate a patient's cells for the treatment, prevention or potentially cure a disease.
- 348 **CAR-T cell therapy (gene-modified cell therapy)** projects use cells that are genetically modified before being reintroduced into the patient with a function gene.
- 265 **DNA or RNA therapeutic** projects which target DNA and RNA to turn off or modify a gene expression that is the root cause of disease.
- 133 **Oncolytic Virus** projects where tumor-seeking viruses may be injected or infused to infect cancerous tumor cells, forcing the cells to release markers that the immune system recognizes as a threat and attacks.

Conclusion

Today's pipeline of potential new medicines is vibrant, diverse, and incredibly promising for patients. The high proportion of projects that have the potential to be first-in-class reflects growing scientific opportunities and demonstrates a commitment to innovation. The continued discovery and development of newer, better treatments saves and improves lives.

As the rapid pace of scientific and technological advances is propelling a new era in biopharmaceutical innovation, it is critical that we ensure a policy and regulatory system that continues to foster the substantial investments needed to support medical advances. Our regulatory system must keep pace with the science and embrace the latest tools to improve the process. Likewise, we need strong intellectual property protections and a market-based delivery system that promotes access and fosters innovation.



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