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THE BIOPHARMACEUTICAL PIPELINE:
Innovative Therapies in Clinical Development

THE PROMISE OF THE PIPELINE

The biopharmaceutical pipeline contains thousands of significant and innovative new treatments with the potential to address unmet medical needs, save lives and improve patients' health. A new report by the Analysis Group, "The Biopharmaceutical Pipeline: Innovative Therapies in Clinical Development," examines the state of the drug development pipeline and provides insights into new approaches researchers are pursuing.

KEY FINDINGS:

- 74 percent of medicines in clinical development are potentially first-in-class medicines, meaning they represent a possible new pharmacological class for treating a medical condition.
- 822 projects – defined as unique molecule-indication combinations – are designated by the U.S. Food and Drug Administration (FDA) as orphan drugs, which is critically important given only 5 percent of rare diseases 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.

The research and development (R&D) process that leads to new treatments and cures for patients is lengthy, challenging and subject to substantial scientific and regulatory uncertainty. In fact, only 12 percent of investigational new medicines entering the clinical trial phase are ultimately approved by the FDA. Our nation's innovative biopharmaceutical companies invest about $75 billion a year to harness new scientific and technological advances in an effort to bring new medical advances forward.

Today, innovative medicines are saving and improving the lives of millions of Americans. They also 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 investments by innovative biopharmaceutical companies support more than 4.4 million jobs across the U.S. economy.

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 made by the biopharmaceutical industry. In the last decade, biopharmaceutical companies have invested over half a trillion dollars in R&D and more than 350 new medicines have been approved by the FDA.

POTENTIAL FIRST-IN-CLASS MEDICINES IN THE PIPELINE

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.

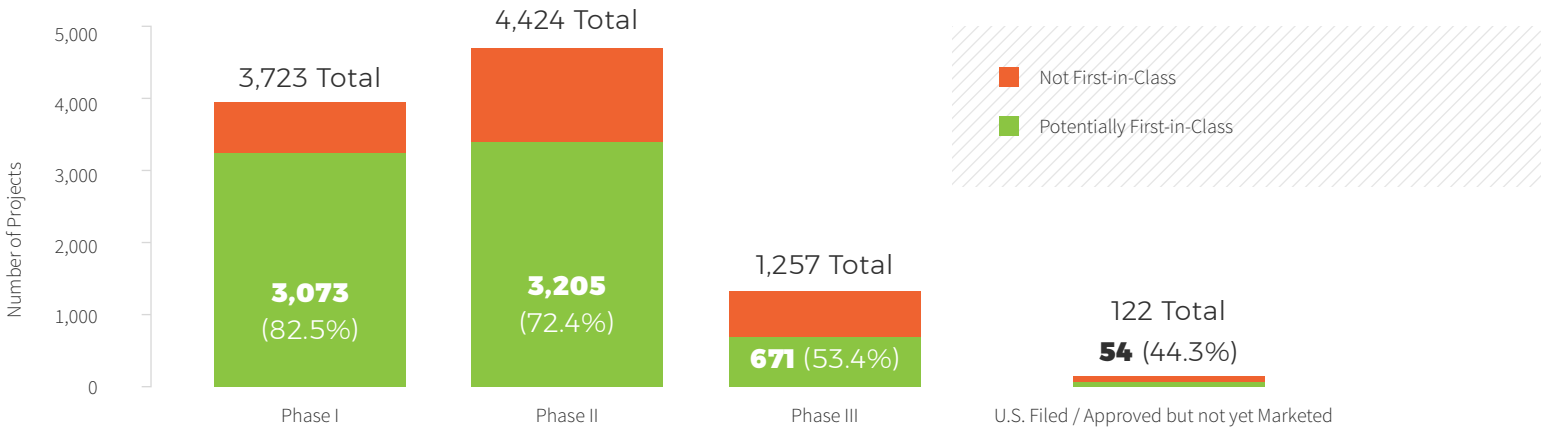
Across the entire clinical development pipeline, 74 percent of projects are potentially first-in-class. When early stage research projects are included, the number rises to 80 percent. High numbers of potential first-in-class medicines are seen in all phases of clinical development, but the percentage decreases for the 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.

FIRST-IN-CLASS MEDICINE IN CLINICAL DEVELOPMENT FOR SELECTED THERAPEUTIC AREAS

Theraputic Areas	Percentage of Projects that are Potentially First-in-Class
CANCER	79%
CARDIOVASCULAR	73%
DIABETES	73%
NEUROLOGY	74%
ALZHEIMER'S DISEASE	86%
PSYCHIATRY	75%

POTENTIAL FIRST-IN-CLASS MEDICINES BY PHASE

An average of 74% of medicines in the clinical pipeline are potential first-in-class medicines



NOTE: Projects were considered potentially first-in-class if they are in a class with no approved medicines available. While there may be more than one investigational drug in the pipeline in a given class, it is difficult to predict which will be approved first so all are counted as potentially first-in-class.

PROMISE IN THE PIPELINE

After three decades of research into the signaling pathways involved in migraines, we are on the cusp of a **new era of migraine treatment**

Fast-acting medicines for **"treatment-resistant" depression** and prevention of suicidal thoughts are in clinical trials

Researchers are advancing game-changing approaches to **fighting blood cancers** by engineering immune system cells to recognize and kill cancer cells

TREATING RARE DISEASES

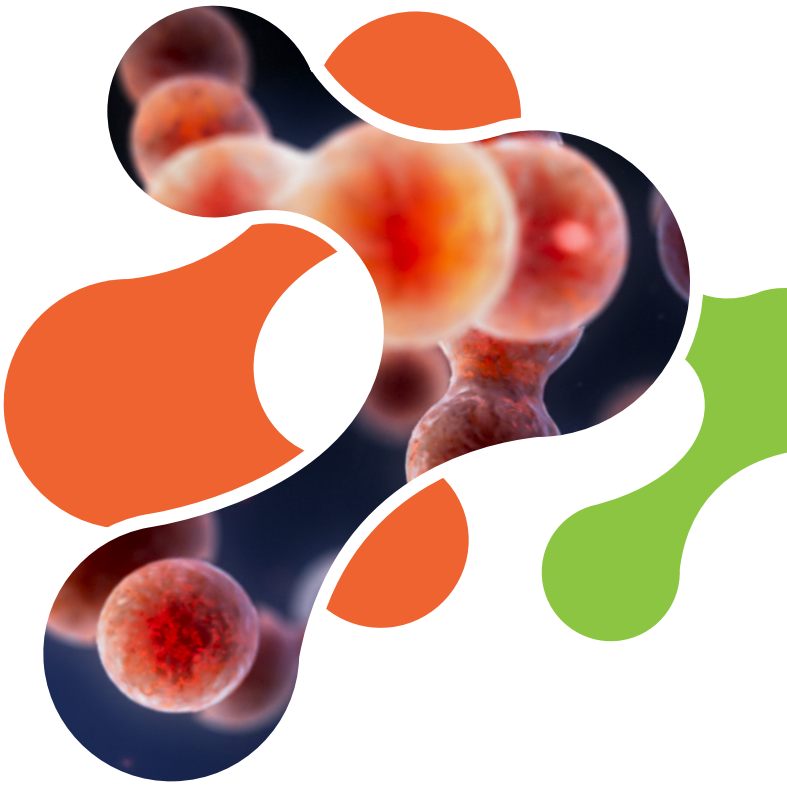
According to the National Institutes of Health (NIH), there are roughly 7,000 rare diseases which, together, affect approximately 30 million people in the United States. Among these diseases, 95 percent have no approved medicines and more than 85 percent are serious or life-threatening. Medicines intended to treat these rare diseases affecting fewer than 200,000 people can be designated as orphan drugs.

The report found 822 orphan drugs are currently in 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 more precisely identify rare diseases. Qualifying for an orphan drug designation does not necessarily mean the product will ultimately be approved as an orphan drug as the investigational medicine must still meet FDA's approval standards. Orphan drugs are being developed across several disease states, including cardiovascular, cancer and neurology.

PIPELINE OF SELECT ORPHAN PROJECTS

CANCER	401
CARDIOVASCULAR	25
IMMUNOLOGY	60
INFECTIONS	32
MUSCULOSKELETAL	26
NEUROLOGY	58

NOTE: Figures represent Phase I,II,III and filed and approved



NOVEL SCIENTIFIC STRATEGIES

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 four platforms highlight a few of the innovative strategies that scientific researchers are using to fight disease:

- **Regenerative Medicine:**
  - 529 projects using **cell therapy** with healthy, functioning cells being used to treat a disease or condition in which the patient's cells are damaged or diseased
  - 202 projects using **gene therapy**, an emerging approach in which a patient's genes are modified to treat or prevent a disease
- 173 **DNA or RNA therapeutics**, targeting DNA and RNA (which carry and transmit genetic information that creates proteins) rather than targeting proteins themselves
- 188 **conjugated monoclonal antibodies** (mAb) which combine a targeted mAb with a cytotoxic agent to attack tumor cells while sparing nearby healthy cells

> "Regenerative medicine is uniquely capable of altering the fundamental mechanisms of disease."
>
> - Alliance for Regenerative Medicine

> "RNA-based therapeutics [...] have great potential to target a large part of the currently undruggable genes and gene products and to generate entirely new therapeutic paradigms in disease, ranging from cancer to pandemic influenza to Alzheimer's disease."
>
> - Steven Dowdy, Nature Biotechnology

> "The century-old dream of creating magic bullets to fight cancer is almost here. Antibody-drug conjugates represent a promising therapeutic approach for advanced cancer patients."
>
> - Cleveland Clinic Innovations

CONCLUSION

Today's pipeline of 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.