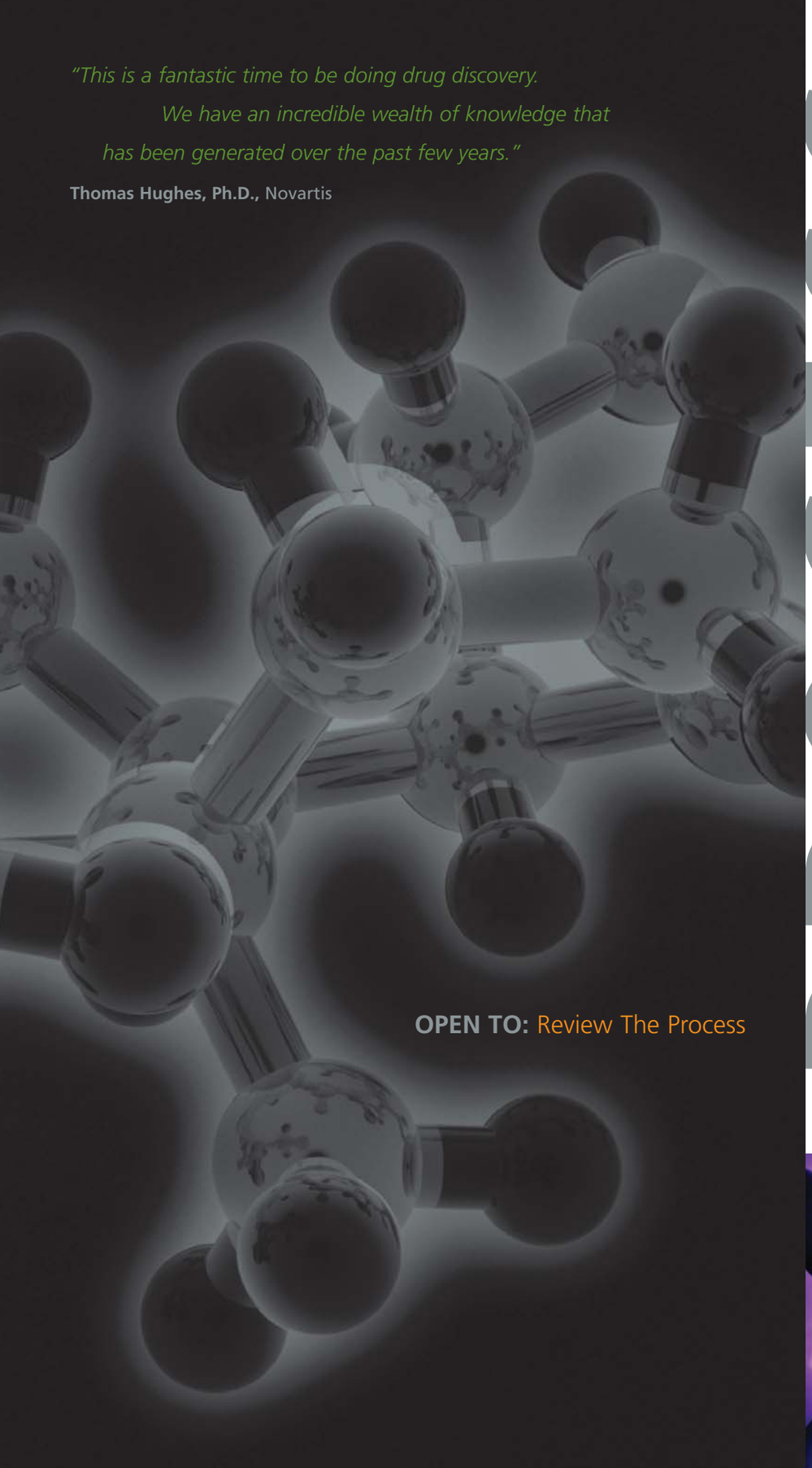
Drug Discovery and Development

UNDERSTANDING THE R&D PROCESS

innovation.org

"This is a fantastic time to be doing drug discovery. We have an incredible wealth of knowledge that has been generated over the past few years."

Thomas Hughes, Ph.D., Novartis



PROCESS

OPEN TO: Review The Process

DRUG DISCOVERY AND DEVELOPMENT: Overview

It is the mission of pharmaceutical research companies to take the path from understanding a disease to bringing a safe and effective new treatment to patients. Scientists work to piece together the basic causes of disease at the level of genes, proteins and cells. Out of this understanding emerge "targets," which potential new drugs might be able to affect (see "How Drugs Work: The Basics" on p. 3). Researchers work to:

- validate these targets,
- discover the right molecule (potential drug) to interact with the target chosen,
- test the new compound in the lab and clinic for safety and efficacy and
- gain approval and get the new drug into the hands of doctors and patients.

This whole process takes an average of **10-15 years.**

PUTTING IT INTO PERSPECTIVE 15 years

It can take up to fifteen years to develop one new medicine from the earliest stages of discovery to the time it is available for treating patients. Many of the drugs coming to the market in 2007 were in the early stages of discovery fifteen years ago, in 1992.

Let's rewind the calendar to 1992 and take a look at what else was happening fifteen years ago.

World Events

- The Federal Republic of Yugoslavia, created in 1918, collapses as Europe officially recognizes the republics of Croatia and Slovenia.
- Signed by Canada, Mexico and the U.S., the North American Free Trade Agreement establishes the world's largest trading bloc.

Top-Grossing Films

- Aladdin
- Home Alone 2: Lost in New York
- Batman Returns

TV

- Jay Leno debuts as host of The Tonight Show.
- The last episode of The Cosby Show airs.
- Ted Turner, founder of CNN, is Time Magazine's Man of the Year.

Politics

- Democrat Bill Clinton defeats incumbent U.S. President George H.W. Bush and businessman H. Ross Perot.

Sports

- Andre Agassi wins Wimbledon.
- The Washington Redskins defeat the Buffalo Bills in Super Bowl XXVI.

Technology

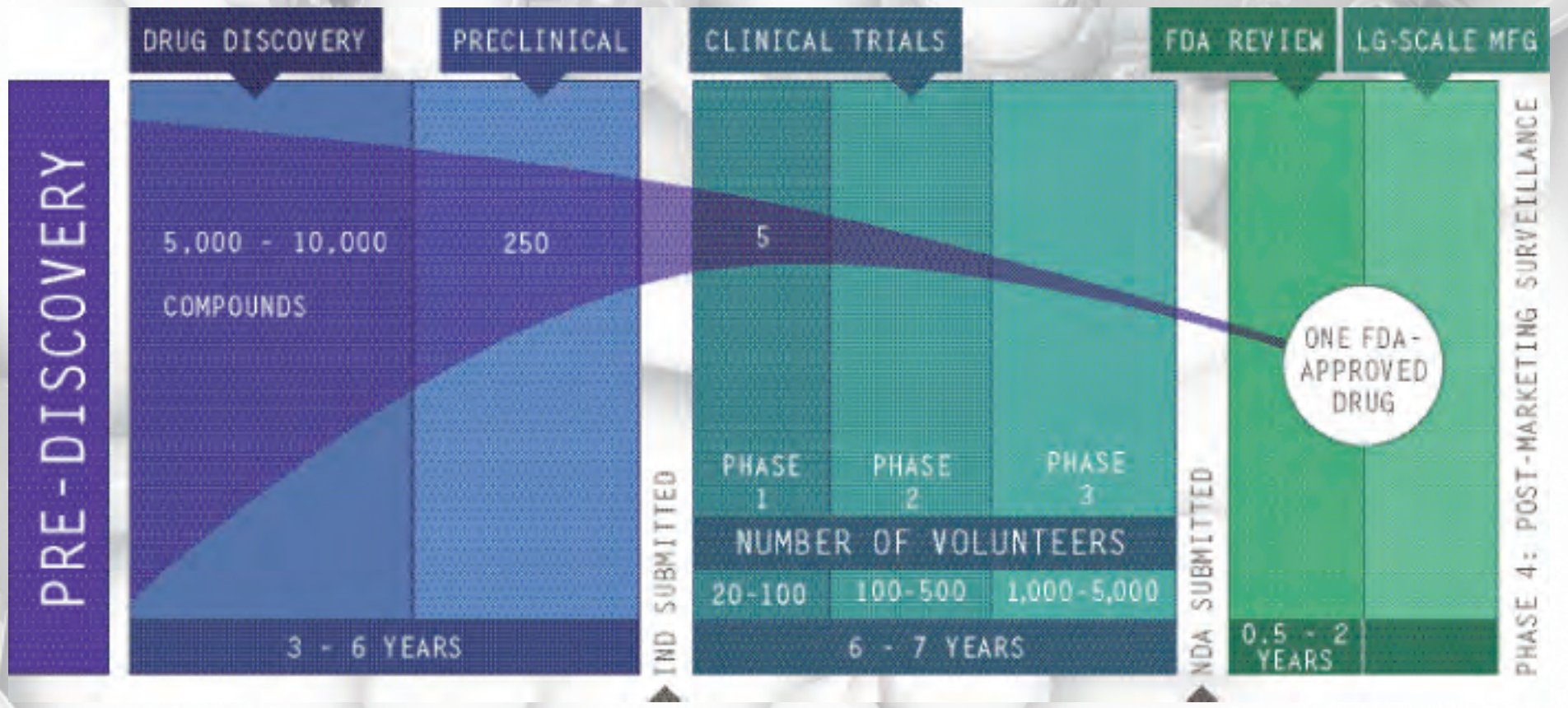
- The Internet Society is chartered, and 1,000,000 host computers are connected in a network. The term "surfing the net" is coined as an increasing number of people begin exploring the online world.
- Compact discs surpass cassette tapes as the preferred medium for recorded music.

DRUG DISCOVERY AND DEVELOPMENT

For the first time in history, scientists are beginning to understand the inner workings of human disease at the molecular level. Recent advances in genomics, proteomics and computational power present new ways to understand illness. The task of discovering and developing safe and effective drugs is even more promising as our knowledge of disease increases. As scientists work to harness this knowledge, it is becoming an increasingly challenging undertaking.

It takes about **10-15 years** to develop one new medicine from the time it is discovered to when it is available for treating patients. The average cost to research and develop each successful drug is estimated to be **$800 million** to **$1 billion**. This number includes the cost of the thousands of failures: For every **5,000-10,000** compounds that enter the research and development (R&D) pipeline, ultimately only one receives approval.

These numbers defy imagination, but a deeper understanding of the R&D process can explain why so many compounds don't make it and why it takes such a large, lengthy effort to get one medicine to patients. Success requires immense resources — the best scientific minds, highly sophisticated technology and complex project management. It also takes persistence and, sometimes, luck. Ultimately, though, the process of drug discovery brings hope and relief to millions of patients.



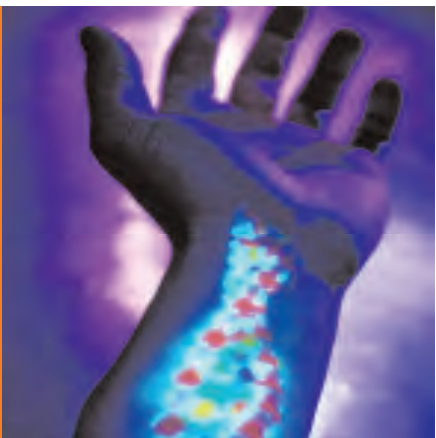
PROCESS

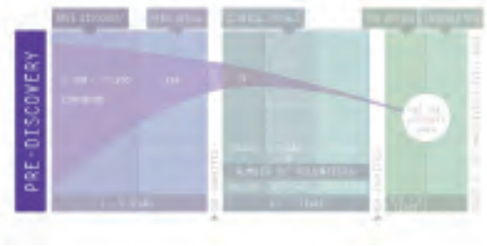
SEQUENCING THE HUMAN GENOME | Why It's a Big Deal

In 2001 the sequencing of the human genome was completed. There are about 20,000-25,000 human genes, made up of 3 billion individual base pairs, the units of DNA. Each gene codes for a protein and these proteins carry out all the functions of the body, laying out how it grows and functions. These proteins can also be involved in disease.

Knowing all the genes, and the proteins they code for gives scientists a full catalogue of options to consider as potential targets for new drugs. It will take time, though, to achieve the potential benefits of this new knowledge. Although we have a list of all the genes, we do not know how they all interact and which are involved in which diseases.

Eventually, scientists hope to discover new drugs that precisely and powerfully prevent and cure disease. The human genome holds incredible potential.





THE DISCOVERY PROCESS INCLUDES ALL EARLY RESEARCH TO IDENTIFY A NEW DRUG CANDIDATE AND TESTING IT IN THE LAB. THE PROCESS TAKES APPROXIMATELY 3-6 YEARS. BY THE END, RESEARCHERS HOPE TO HAVE A PROMISING CANDIDATE DRUG TO TEST IN PEOPLE.

THE DISCOVERY PROCESS

Pre-discovery
Understand the disease

Before any potential new medicine can be discovered, scientists work to understand the disease to be treated as well as possible, and to unravel the underlying cause of the condition. They try to understand how the genes are altered, how that affects the proteins they encode and how those proteins interact with each other in living cells, how those affected cells change the specific tissue they are in and finally how the disease affects the entire patient. This knowledge is the basis for treating the problem.

Researchers from government, academia and industry all contribute to this knowledge base. However, even with new tools and insights, this research takes many years of work and, too often, leads to frustrating dead ends. And even if the research is successful, it will take many more years of work to turn this basic understanding of what causes a disease into a new treatment.

"Some ideas may just stay on paper forever, but others have a way forward to make it into a pill, into a bottle at the pharmacy."

Debra Luffer-Atlas, Ph.D., Eli Lilly and Company

PUBLIC AND PRIVATE Collaborations

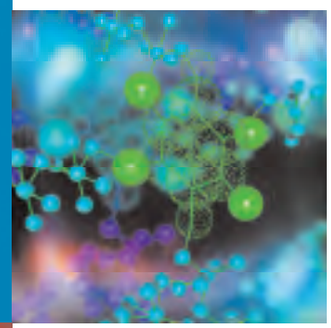
Modern drug discovery is the product of cooperation. Many sectors contribute, particularly in building the basic science foundations. Both public and private organizations play unique but increasingly interdependent roles in translating basic research into medicine.

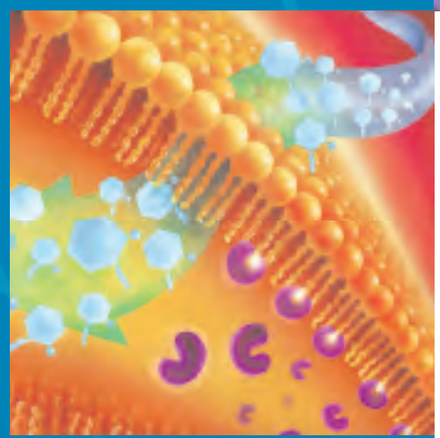
- Major biopharmaceutical companies are the primary source of R&D funding for new medicines, both for projects in their own laboratories as well as for research licensed from other sectors.
- Smaller companies also drive innovation, conducting basic research, drug discovery, preclinical experiments and, in some cases, clinical trials.
- The National Institutes of Health (NIH) provides leadership and funding support to universities, medical schools, research centers and other nonprofit institutions, and stimulates basic research and early-stage development of technologies that enable further targeted drug discovery and development.

The cells in our bodies carry out complex molecular reactions to perform every function — from digesting your lunch, to moving your finger, to regulating cell growth and transmitting thoughts in your brain. One type of molecule interacts with another which, in turn, affects another, and so on down the line. These cascades of molecular changes are called chemical pathways.

In many different and extremely complex ways, these pathways are involved in disease. A mistake in one reaction might stop an important protein from being produced or lead to too much production. These molecular imbalances can have big consequences. Maybe they will cause extra cells to grow — like in cancer — or perhaps cause the person's body to not produce enough insulin — like in diabetes.

Drug molecules affect these pathways by interacting with certain molecules along the pathway, making them more active or less active, or changing their activity all together.





Target Identification
Choose a molecule to target with a drug

Once they have enough understanding of the underlying cause of a disease, pharmaceutical researchers select a "target" for a potential new medicine. A target is generally a single molecule, such as a gene or protein, which is involved in a particular disease. Even at this early stage in drug discovery it is critical that researchers pick a target that is "drugable," i.e., one that can potentially interact with and be affected by a drug molecule.

Target Validation
Test the target and confirm its role in the disease

After choosing a potential target, scientists must show that it actually is involved in the disease and can be acted upon by a drug. Target validation is crucial to help scientists avoid research paths that look promising, but ultimately lead to dead ends. Researchers demonstrate that a particular target is relevant to the disease being studied through complicated experiments in both living cells and in animal models of disease.

Drug Discovery
Find a promising molecule (a "lead compound") that could become a drug

Armed with their understanding of the disease, scientists are ready to begin looking for a drug. They search for a molecule, or "lead compound," that may act on their target to alter the disease course. If successful over long odds and years of testing, the lead compound can ultimately become a new medicine.

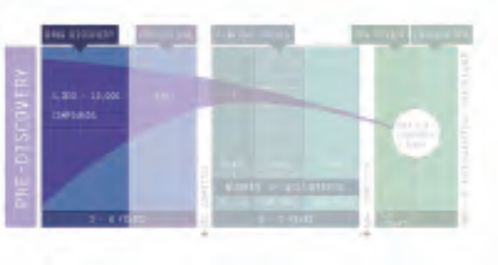
There are a few ways to find a lead compound:

Nature: Until recently, scientists usually turned to nature to find interesting compounds for fighting disease. Bacteria found in soil and moldy plants both led to important new treatments, for example. Nature still offers many useful substances, but now there are other ways to approach drug discovery.

De novo: Thanks to advances in chemistry, scientists can also create molecules from scratch. They can use sophisticated computer modeling to predict what type of molecule may work.

High-throughput Screening: This process is the most common way that leads are usually found. Advances in robotics and computational power allow researchers to test hundreds of thousands of compounds against the target to identify any that might be promising. Based on the results, several lead compounds are usually selected for further study.

Biotechnology: Scientists can also genetically engineer living systems to produce disease-fighting biological molecules.



"If at the end of my career, I can look back and know that something I did made a difference in one patient somewhere in the world, that'll be more satisfying and more gratifying than anything I can possibly imagine."

Jonathan Yingling, Ph.D., Eli Lilly and Company

Early Safety Tests
Perform initial tests on promising compounds

Lead compounds go through a series of tests to provide an early assessment of the safety of the lead compound. Scientists test **A**bsorption, **D**istribution, **M**etabolism, **E**xcretion and **Tox**icological (ADME/Tox) properties, or "pharmacokinetics," of each lead. Successful drugs must be:

- absorbed into the bloodstream,
- distributed to the proper site of action in the body,
- metabolized efficiently and effectively,
- successfully excreted from the body and
- demonstrated to be not toxic.

These studies help researchers prioritize lead compounds early in the discovery process. ADME/Tox studies are performed in living cells, in animals and via computational models.

Lead Optimization
Alter the structure of lead candidates to improve properties

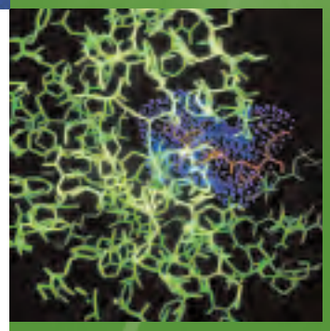
Lead compounds that survive the initial screening are then "optimized," or altered to make them more effective and safer. By changing the structure of a compound, scientists can give it different properties. For example, they can make it less likely to interact with other chemical pathways in the body, thus reducing the potential for side effects.

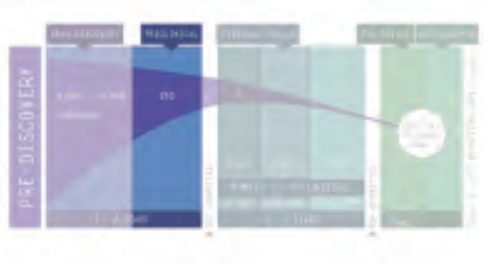
Hundreds of different variations or "analogues" of the initial leads are made and tested. Teams of biologists and chemists work together closely: The biologists test the effects of analogues on biological systems while the chemists take this information to make additional alterations that are then retested by the biologists. The resulting compound is the candidate drug.

Even at this early stage, researchers begin to think about how the drug will be made, considering formulation (the recipe for making a drug, including inactive ingredients used to hold it together and allow it to dissolve at the right time), delivery mechanism (the way the drug is taken – by mouth, injection, inhaler) and large-scale manufacturing (how you make the drug in large quantities).

LEAD OPTIMIZATION
at the molecular level

New techniques have revolutionized the ability of researchers to optimize potential drug molecules. Thanks to technologies such as magnetic resonance imaging and X-ray crystallography, along with powerful computer modeling capabilities, chemists can actually "see" the target in three dimensions and design potential drugs to more powerfully bind to the parts of the target where they can be most effective. In addition, new chemistry techniques help scientists to synthesize the new compounds quickly.





"The number of people involved in getting a drug to the first patient is a small phonebook. It's hundreds to even a thousand or two thousand, depending on the nature of the work. It requires people from a whole set of different disciplines, ranging from a geneticist who may be that person who makes the first link of a gene with a disease, to the chemist who tried to understand how to make a chemical that will interact with a protein, that a biochemist will have isolated, to a pharmacist who will figure out how to take that chemical and put it into some kind of delivery device, what we call a pill or injection, to computer scientists who work to try to predict how that drug is going to behave in a patient or in a large population, and so on. The set of disciplines is immense."

John Leonard, M.D., Abbott

Preclinical Testing

Lab and animal testing to determine if the drug is safe enough for human testing

With one or more optimized compounds in hand, researchers turn their attention to testing them extensively to determine if they should move on to testing in humans.

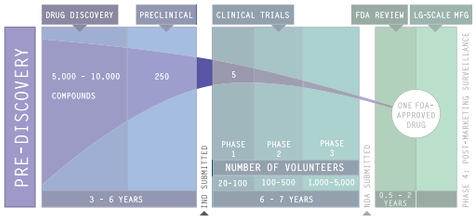
Scientists carry out *in vitro* and *in vivo* tests. *In vitro* tests are experiments conducted in the lab, usually carried out in test tubes and beakers ("vitro" is "glass" in Latin) and *in vivo* studies are those in living cell cultures and animal models ("vivo" is "life" in Latin). Scientists try to understand how the drug works and what its safety profile looks like. The U.S. Food and Drug Administration (FDA) requires extremely thorough testing before the candidate drug can be studied in humans.

During this stage researchers also must work out how to make large enough quantities of the drug for clinical trials. Techniques for making a drug in the lab on a small scale do not translate easily to larger production. This is the first scale up. The drug will need to be scaled up even more if it is approved for use in the general patient population.

At the end of several years of intensive work, the discovery phase concludes. After starting with approximately 5,000 to 10,000 compounds, scientists now have winnowed the group down to between one and five molecules, "candidate drugs," which will be studied in clinical trials.

"The challenge of finding a new drug is an incredible thing. You're trying to solve a complex disease with a single molecule. It's an incredible challenge. We employ technologies that are just unbelievable in their depth and their complexity. At the end of day, we do this to bring some comfort to people who are suffering and dealing with the anguish and despair of a chronic disease. It's to bring some hope to them."

Thomas E. Hughes, Ph.D., Novartis



"I think we've only begun to scratch the surface in our understanding of disease and the way we're going to be able to treat diseases. Many of us that are in the industry now... I don't think we can even conceive of where it's all going to go in the future, but there's a long, long way to go. We've only just begun."

Charles Gombar, Ph.D., Wyeth

A CANDIDATE DRUG MUST GO THROUGH EXTENSIVE STUDIES IN HUMANS, AND IT MUST PROVE TO BE SAFE AND EFFECTIVE BEFORE THE FDA WILL APPROVE IT. THIS PROCESS INVOLVES A SERIES OF CLINICAL TRIALS, EACH WITH ITS OWN SPECIFIC GOALS AND REQUIREMENTS. PHYSICIANS CARRY OUT EACH TRIAL WORKING WITH PATIENTS IN HOSPITALS, OFFICES AND CLINICS, AND COORDINATING CLOSELY WITH THE SPONSOR COMPANY. THE CLINICAL TRIALS PROCESS IS BOTH EXPENSIVE AND TIME-CONSUMING, AND ENDS MORE OFTEN IN FAILURE THAN SUCCESS. FROM START TO FINISH IT TAKES AN AVERAGE OF 6-7 YEARS.

THE DEVELOPMENT PROCESS

Investigational New Drug (IND) Application and Safety

File IND with the FDA before clinical testing can begin; ensure safety for clinical trial volunteers through an Institutional Review Board

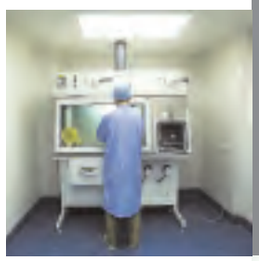
Before any clinical trial can begin, the researchers must file an Investigational New Drug (IND) application with the FDA. The application includes the results of the preclinical work, the candidate drug's chemical structure and how it is thought to work in the body, a listing of any side effects and manufacturing information. The IND also provides a detailed clinical trial plan that outlines how, where and by whom the studies will be performed.

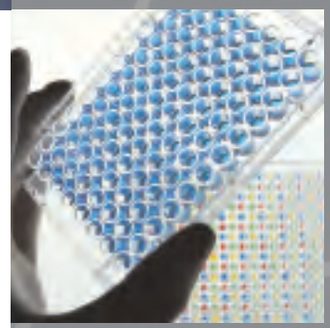
The FDA reviews the application to make sure people participating in the clinical trials will not be exposed to unreasonable risks.

In addition to the IND application, all clinical trials must be reviewed and approved by the Institutional Review Board (IRB) at the institutions where the trials will take place. This process includes the development of appropriate informed consent, which will be required of all clinical trial participants.

Statisticians and others are constantly monitoring the data as it becomes available. The FDA or the sponsor company can stop the trial at any time if problems arise. In some cases a study may be stopped because the candidate drug is performing so well that it would be unethical to withhold it from the patients receiving a placebo or another drug.

Finally, the company sponsoring the research must provide comprehensive regular reports to the FDA and the IRB on the progress of clinical trials.





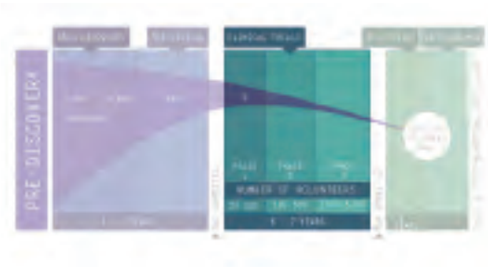
CLINICAL TRIAL DESIGN

An incredible amount of thought goes into the design of each clinical trial. To provide the highest level of confidence in the validity of results, many drug trials are placebo-controlled, randomized and double-blinded. What does that mean?

- Placebo-controlled: Some subjects will receive the new drug candidate and others will receive a placebo. (In some instances, the drug candidate may be tested against another treatment rather than a placebo.)
- Randomized: Each of the study subjects in the trial is assigned randomly to one of the treatments.
- Double-blinded: Neither the researchers nor the subjects know which treatment is being delivered until the study is over.

This method of testing provides the best evidence of any direct relationship between the test compound and its effect on disease because it minimizes human error.

The number of subjects enrolled in a trial (the "power" of the trial) also has to be carefully considered: In general, enrolling more subjects results in greater statistical significance of the results, but is also more expensive and difficult to undertake.



PHASE 0, 2A AND 2B TRIALS

Scientists are always working to identify ways to improve the R&D process and exploring new methods to help reduce the costs and length of clinical trials. Restructured trials help researchers get as much information as possible in the earliest stages and eliminate compounds that are more likely to fail only after longer, more expensive trials.

Phase 0 Trial: The FDA has recently endorsed "microdosing," or the "Phase 0 trial," which allows researchers to test a small drug dose in fewer human volunteers to quickly weed out drug candidates that are metabolically or biologically ineffective.

Phase 2a and 2b Trials: Sometimes combined with a Phase 1 trial, a Phase 2a trial is aimed not only at understanding the safety of a potential drug, but also getting an early read on efficacy and dosage in a small group of patients. The resulting Phase 2b trial would be designed to build on these results in a larger group of patients for the sake of designing a rigorous and focused Phase 3 trial.

Phase 1 Clinical Trial
Perform initial human testing in a small group of healthy volunteers

In Phase 1 trials the candidate drug is tested in people for the first time. These studies are usually conducted with about 20 to 100 healthy volunteers. The main goal of a Phase 1 trial is to discover if the drug is safe in humans. Researchers look at the pharmacokinetics of a drug: How is it absorbed? How is it metabolized and eliminated from the body? They also study the drug's pharmacodynamics: Does it cause side effects? Does it produce desired effects? These closely monitored trials are designed to help researchers determine what the safe dosing range is and if it should move on to further development.

Phase 2 Clinical Trial
Test in a small group of patients

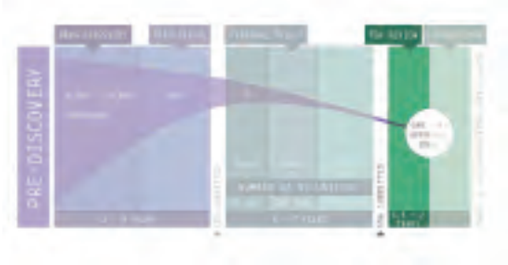
In Phase 2 trials researchers evaluate the candidate drug's effectiveness in about 100 to 500 patients with the disease or condition under study, and examine the possible short-term side effects (adverse events) and risks associated with the drug. They also strive to answer these questions: Is the drug working by the expected mechanism? Does it improve the condition in question? Researchers also analyze optimal dose strength and schedules for using the drug. If the drug continues to show promise, they prepare for the much larger Phase 3 trials.

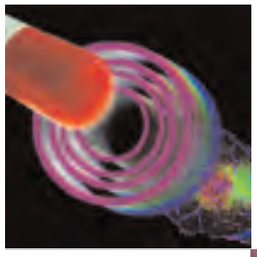
Phase 3 Clinical Trial
Test in a large group of patients to show safety and efficacy

In Phase 3 trials researchers study the drug candidate in a larger number (about 1,000-5,000) of patients to generate statistically significant data about safety, efficacy and the overall benefit-risk relationship of the drug. This phase of research is key in determining whether the drug is safe and effective. It also provides the basis for labeling instructions to help ensure proper use of the drug (e.g., information on potential interactions with other medicines).

Phase 3 trials are both the costliest and longest trials. Hundreds of sites around the United States and the world participate in the study to get a large and diverse group of patients. Coordinating all the sites and the data coming from them is a monumental task.

During the Phase 3 trial (and even in Phases 1 and 2), researchers are also conducting many other critical studies, including plans for full-scale production and preparation of the complex application required for FDA approval.





New Drug Application (NDA) and Approval
Submit application for approval to FDA

Once all three phases of the clinical trials are complete, the sponsoring company analyzes all of the data. If the findings demonstrate that the experimental medicine is both safe and effective, the company files a New Drug Application (NDA) — which can run 100,000 pages or more — with the FDA requesting approval to market the drug. The NDA includes all of the information from the previous years of work, as well as the proposals for manufacturing and labeling of the new medicine.

FDA experts review all the information included in the NDA to determine if it demonstrates that the medicine is safe and effective enough to be approved (see sidebar — "How does the FDA decide to approve a new drug?"). Following rigorous review, the FDA can either 1) approve the medicine, 2) send the company an "approvable" letter requesting more information or studies before approval can be given, or 3) deny approval.

Review of an NDA may include an evaluation by an advisory committee, an independent panel of FDA-appointed experts who consider data presented by company representatives and FDA reviewers. Committees then vote on whether the FDA should approve an application, and under what conditions. The FDA is not required to follow the recommendations of the advisory committees, but often does.

"I will never forget seeing the patients explain their experience because they were taking our drugs. That's wonderful. That's a gift. And that is something that nobody can understand if you haven't experienced it. That is the benefit that working in this industry provides. And it has been wonderful for me."

Karen Ragland, B.S.N., M.S., Otsuka Pharmaceutical Development & Commercialization, Inc.

How does the FDA decide to approve a new drug?

BENEFIT VS. RISK

After close to a decade of testing, the company files a New Drug Application (NDA) with the FDA. Reported in the NDA are all the data gathered from all studies of the potential new drug, including the preclinical as well as clinical findings. The FDA then scrutinizes all the data carefully to determine if the medicine should be approved. In particular, it uses the information in the NDA to try to address three major concerns:

1) Because no drug has zero risk, the FDA must determine whether the benefits of the drug outweigh the risks, i.e., is the drug effective for its proposed use, and has an acceptable balance between benefits and risks been achieved?

2) Based on its assessment of risk and benefit, the FDA must decide what information the package insert should contain to guide physicians in the use of the new drug.

3) Finally, the FDA must assess whether the methods used to manufacture the drug and ensure its quality are adequate to preserve the drug's identity, strength and purity.

DIVERSE BACKGROUNDS, Common Goal

"I was born in Africa. I was fortunate in the sense that I was born into a middle-class family and had access to good health care and education. There were, however, many others that were not so fortunate. So growing up, I had always been interested in working in health care. Medicines had always fascinated me and captured my imagination because I had seen first-hand on so many occasions where they can be life-saving and life-transforming. So in a sense, it was kind of natural for me to gravitate towards pharmacy and to learn about how medicines are made and how they work."

Sisay Gebrekidan, Ph.D.
GlaxoSmithKline

"My calling to the pharmaceutical industry has been a personal one. When I was a child, I had a disease called rheumatic fever that came from strep throat. It had an effect on my heart and, as a child — in third grade for me — I was unable to play with other children. In fact, I had to lie in a bed for months and be carried. It was a medicine that I took that allowed me to get up again, and it was a medicine that the company that I work for today made. That's why I joined the pharmaceutical industry."

Andrew Dahlem, Ph.D.
Eli Lilly and Company

Manufacturing

Going from small-scale to large-scale manufacturing is a major undertaking. In many cases, companies must build a new manufacturing facility or reconstruct an old one because the manufacturing process is different from drug to drug. Each facility must meet strict FDA guidelines for Good Manufacturing Practices (GMP).

Making a high-quality drug compound on a large scale takes great care. Imagine trying to make a cake, for example, on a large scale — making sure the ingredients are evenly distributed in the mix, ensuring that it heats evenly. The process to manufacture most drugs is even more complicated than this. There are few, if any, other businesses that require this level of skill in manufacturing.

Ongoing Studies and Phase 4 Trials

Research on a new medicine continues even after approval. As a much larger number of patients begin to use the drug, companies must continue to monitor it carefully and submit periodic reports, including cases of adverse events, to the FDA.

In addition, the FDA sometimes requires a company to conduct additional studies on an approved drug in "Phase 4" studies. These trials can be set up to evaluate long-term safety or how the new medicine affects a specific subgroup of patients.

"I find it very exciting to be involved with the drug in its final stages... after so many years of waiting. The patients are finally getting access to the drug that potentially is going to help them."

Martha Brumfield, Ph.D., Pfizer, Inc.

Conclusion

The discovery and development of new medicines is a long, complicated process. Each success is built on many, many prior failures. Advances in understanding human biology and disease are opening up exciting new possibilities for breakthrough medicines. At the same time, researchers face great challenges in understanding and applying these advances to the treatment of disease. These possibilities will grow as our scientific knowledge expands and becomes increasingly complex. Research-based pharmaceutical companies are committed to advancing science and bringing new medicines to patients.

"Patients are not an abstract concept to those who work in research. We know patients, our parents are patients, our friends are patients, our children are patients and sometimes we are patients."

Andrew Dahlem, Ph.D., Eli Lilly and Company

"I think there's a tendency for people to take medical advances for granted. And it's in part because we, in our society, have had a run of incredible successes over the last 20 to 30 years. And if one grows up in a society that is defined by that success, it's easy to lose sight of what makes those successes possible. And whether it's the scientific training that's necessary, the resources that are important to fund these teams and let them do their work, the participation in clinical trials of patients... if there's not a collective awareness of all that makes this possible, it's entirely possible that this light that we have could be snuffed out."

John Leonard, M.D., Abbott

DISCOVERY

Pre-discovery
Goal: Understand the disease and choose a target molecule.
How: Scientists in pharmaceutical research companies, government, academic and for-profit research insititutions contribute to basic research.

3 - 6 YEARS

Discovery
Goal: Find a drug candidate.
How: Create a new molecule or select an existing molecule as the starting point. Perform tests on that molecule and then optimize (change its structure) it to make it work better.

Preclinical
Goal: Test extensively to determine if the drug is safe enough for human testing.
How: Researchers test the safety and effectiveness in the lab and in animal models.

DEVELOPMENT

6 - 7 YEARS

IND
Goal: Obtain FDA approval to test the drug in humans.
How: FDA reviews all preclinical testing and plans for clinical testing to determine if the drug is safe enough to move to human trials.

Clinical Trials
Goal: Test in humans to determine if the drug is safe and effective.
How: Candidate drug is tested in clinical setting in three phases of trials, beginning with tests in a small group of healthy volunteers and moving into larger groups of patients.

0.5 - 2 YEARS

Review
Goal: FDA reviews results of all testing to determine if the drug can be approved for patients to use.
How: The FDA reviews hundreds of thousands of pages of information, including all clinical and preclinical findings, proposed labeling and manufacturing plans. They may solicit the opinion of an independent advisory committee.

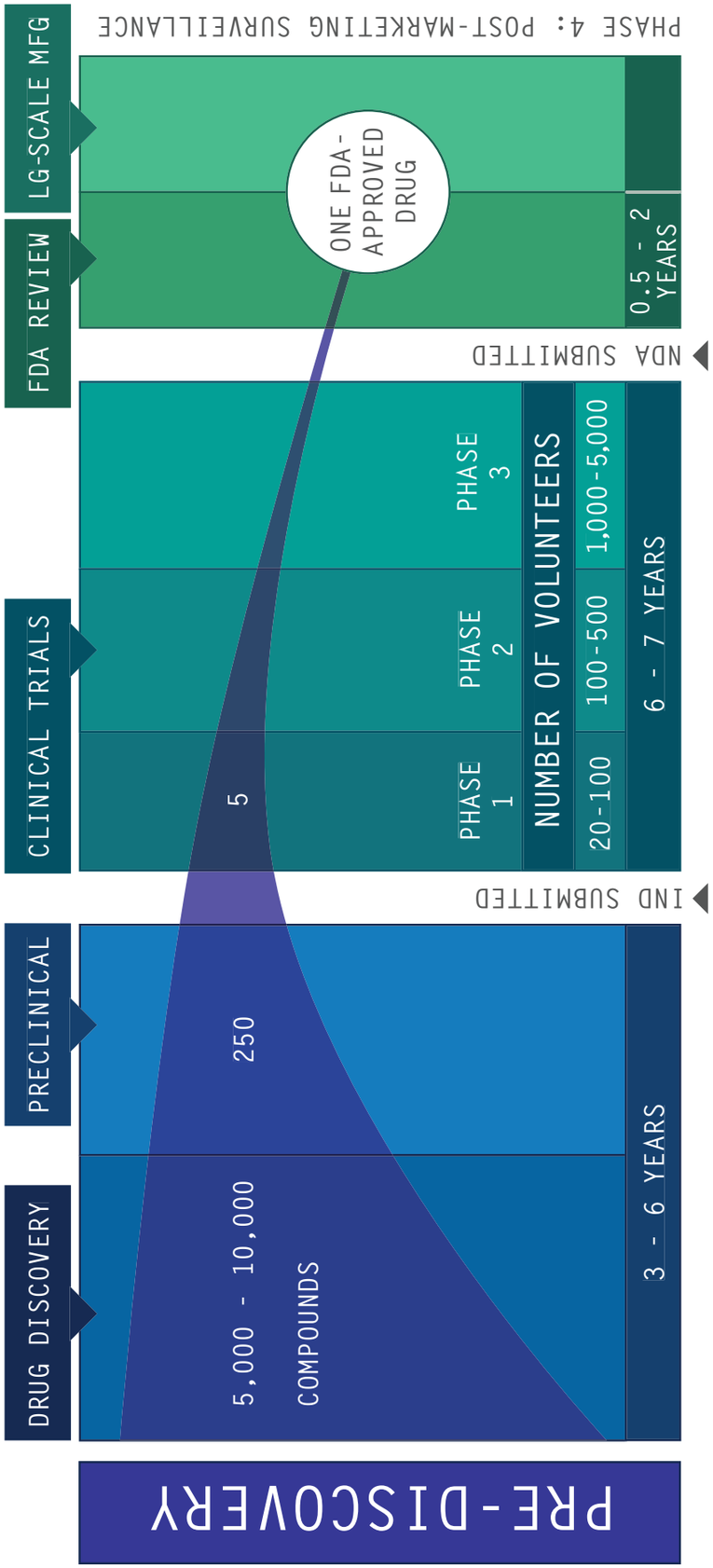
Manufacturing
Goal: Formulation, scale up and production of the new medicine.

Ongoing Studies
Goal: Monitor the drug as it is used in the larger population to catch any unexpected serious side effects.

TOTAL
How much: $800 million – $1 billion
How long: 10 – 15 years

PHARMACEUTICAL RESEARCH & DEVELOPMENT

PROCESS



REFERENCES

J.A. DiMasi, "New Drug Development in the United States from 1963-1999," Clinical Pharmacology and Therapeutics 69, no. 5 (2001): 286-296.

J.A. DiMasi, R.W. Hansen and H.G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs," Journal of Health Economics 22 (2003): 151-185.

Pharmaceutical Research and Manufacturers of America, based on data from Tufts University, Tufts Center for the Study of Drug Development (1995).

Meadows, M. (2002) The FDA's Drug Review Process: Ensuring Drugs are Safe and Effective. FDA Consumer 36: (revised September 2002, http://www.fda.gov/fdac/features/2002/402_drug.html)

Pharmaceutical Research and Manufacturers of America, Pharmaceutical Industry Profile 2006, (Washington, DC: PhRMA, March 2006).

Tufts Center for the Study of Drug Development, "Average Cost to Develop a New Biotechnology Product Is $1.2 Billion, According to the Tufts Center for the Study of Drug Development," 9 November 2006, http://csdd.tufts.edu/NewsEvents/NewsArticle.asp?newsid=69 (accessed 18 December 2006).

Interviews with researchers.

For more information, please visit:

innovation.org/insideRandD

innovation.org

PhRMA
950 F Street, NW
Washington, DC 20004

February 2007