Academia and Industry

Working together towards a common goal – advancing patient care
Welcoming message

In 1955, at the University of Pittsburgh, Dr. Jonas Salk discovered the first vaccine effective against polio. In the most successful partnership of its time, the University, the US Government, and a group of pharmaceutical companies collaborated to develop the vaccine from a laboratory breakthrough to a safe and effective vaccine, overcoming one of the world’s most feared diseases. That kind of collaboration has been repeated thousands of times – in fact, most advances in modern medicine are rooted in collaborations between research-oriented pharma companies and academic institutions of all sizes and types. Each has a vital role to play in making medical progress, and neither can succeed without the help of the other.

We know that on many campuses today, there is considerable discussion, and even controversy, about the appropriate interactions between pharmaceutical companies and academia, especially surrounding the development and marketing of new therapies. We’re listening and responding to these concerns. And while we know that academia and industry will differ on some issues, we share a lot of common ground.

This brochure illustrates how collaborations between academic institutions and pharma companies can result in actions that benefit patients. It is not meant to convince you that one group or the other is always right, but rather to discuss the issues and demonstrate, through case histories, how interdependent we are.

The partnerships between academia and biopharmaceutical companies have yielded great strides in medicine. That said, there are still billions of people with serious unmet medical needs. Only by understanding the process that turns a scientific discovery into an approved medicine, ready to be safely and effectively used by patients, can we hope to meet these unmet needs, and to bring better health to many more of the world’s people.
From illness to health...
How a therapy emerges from bench to bedside

Once an unmet therapeutic need is recognized, research can lead to an understanding of the underlying mechanism of the disease at the molecular level. It is this basic research that makes possible the discovery of new therapies that can alter or prevent the progression of the disease.1

A disease process often involves multiple pathways; intervening in any one of them may have a positive impact. Once a mechanism of action is understood, the next step is to learn how to alter that process. Thousands of compounds are screened to identify a few lead candidates that may have the desired effect.1

Those candidates that show promise are then developed and optimized through preclinical testing to establish desired activity and mechanism of action, assess probable safety, and assess their potential for efficacy in humans.1 Therapies are also evaluated to assess whether they can be reliably and consistently manufactured.
To demonstrate safety and efficacy in humans, clinical studies, planned with close regulatory oversight, incrementally introduce the therapy to patient populations.\textsuperscript{1,3} When studies show that there is an acceptable balance of safety and efficacy, or risk vs benefit, regulatory approval may be requested.\textsuperscript{1}

Once approved by the Food and Drug Administration (FDA), the therapy is produced and distributed for use in the general population according to the FDA-approved labelling. All communications developed to educate doctors and consumers about the product’s risks and benefits must strictly adhere to the FDA regulations and guidelines.\textsuperscript{1}

Support for a therapy’s appropriate use is a responsibility that endures for the life of the drug – even beyond its patent expiration. This support may include continuous safety monitoring and communications with the many stakeholders within the medical community and with consumers.\textsuperscript{1}
Synergy for a common goal: advancing patient care

Academia

Over the past 100 years scientific advances from academia have contributed to our increasing life expectancy. These enabling types of discoveries, ranging from the discovery of penicillin in the laboratory to the more recent molecular sequencing of the human genome, have led, in turn, to continuing breakthroughs in modern medicine.

The success of academia is the result of the unconstrained pursuit of knowledge about a particular disease or pathway. With multiple sources of funding for basic research, academia has the intellectual freedom to explore and discover. Furthermore, competition between investigators who are working toward a common goal constantly expands the knowledge base.

Information gained from basic scientific research on the fundamental mechanisms of disease, the discovery of new genes and cellular mechanisms, and the relationship between protein structure and biologic function have supported the discovery of new drugs and biologic treatments. Sequencing of the human genome has shown value for predicting drug response and holds the promise of optimizing personalized therapy.

Still, a great number of unmet needs remain – prevention of or cures for diabetes, cancers, Alzheimer’s disease, multiple sclerosis, Parkinson’s disease, immune disorders, and relief for pain, to name just a few areas where breakthroughs in basic science research are needed to start industry on the path of development of new therapies.

Government funding, monitoring, and drug approval

Funding provided by the government allows for basic science research into a particular target or pathway, which increases existing knowledge and may ultimately result in new drug discoveries.

Oversight from regulatory authorities covers clinical testing and continues for the life of the product. Monitoring clinical development is a primary task of the FDA. Monitoring is performed throughout the entire clinical trial process to assess safety and efficacy, protect trial participants, and guide the proper management of clinical trial data.
Industry

Industry translates scientific discoveries into commercially viable therapies through the work of the many scientists employed by industry.

Pharmaceutical innovation can be traced back to the early 1800s, with the discovery of ether as an anesthetic. Since then, tremendous strides in patient care have been made, due in large part to the ability of industry to put academic discoveries into practice.

Industry brings together the considerable human and financial resources necessary to translate an academic theory or discovery into a therapeutic entity. The inherent structure of pharmaceutical companies allows them to make targeted investments in therapies and to introduce them into clinical practice. Then, industry continues to support their appropriate use to advance the state of care.

Development of a therapeutic entity is a costly and lengthy process with significant risks that, in our society, is incentivized with the potential for profit. This process of commercialization contributes to better therapeutic options, improved patient outcomes, and advances in scientific knowledge.

Profits, in turn, fund future cycles of research and development that will be needed to continue to build on breakthroughs in academic research and to introduce new therapies.

In the United States, ultimate approval of a drug rests with the FDA. Once approved and marketed, governmental agencies, in coordination with industry, continue to support its appropriate use with safety monitoring. The FDA also maintains regulatory oversight of all marketing and sales initiatives, including all print, Web, and TV promotion, which must all adhere to the approved product label information.
Step 1.
Fundamental disease research and isolation of the target for intervention

Academia performs the basic science research that is responsible for broad advances in the knowledge of how the body functions at the cellular level and for fundamental discoveries about the mechanism of disease. This research can identify targets for an intervention that may change the natural course of disease by altering, disrupting, or enhancing the process. Understanding the pathway for one condition may provide insights into pathways of other diseases that function in a similar way. The elucidation of this process and the isolation of potential targets provide the basis for industry’s efforts to discover therapies that have the potential to advance patient care.

Industry builds upon the work of academia to translate research into the discovery and development of commercial products that can have an impact on patient care. Industry has a large store of information about how certain molecules affect biological processes. Using this knowledge, and often working in concert with academia, industry creates compounds or biologic entities with the potential to target the process that has been identified.
### Step 2.
Screen potential therapeutic options to identify lead candidate

Thousands of compounds are isolated, synthesized, or bioengineered in order to develop a lead compound with the greatest potential to affect the identified target.² With its extensive library of compounds and knowledge of their impact in the body, industry can isolate candidates with the most promise and a low potential for unintended effects.² The process of selecting and optimizing discovery of lead compounds requires the knowledge and use of many advanced technologies.²,³

**Biotherapeutics**, including recombinant proteins, vaccines, antibodies, and engineered RNAi antibodies, are screened and bioengineered to address targets that small molecules cannot attack.

### Step 3.
Develop and optimize lead candidate

In order to optimize risk/benefit, a candidate must be tested in vitro and in vivo to assess its activity, potency, selectivity, and toxicity. The compound is also evaluated for solubility, bioavailability, proof of free drug in the blood, and safety. Only if it meets specific criteria will it be considered for testing in humans. Additional molecules are also synthesized based on the lead compound. This costly and involved process is known as preclinical development, a stage that generally takes 1 to 3 years.⁵

### Step 4.
Perform and conduct clinical testing in humans

Clinical testing is conducted to demonstrate safety and efficacy. The FDA plays an important role in guiding the design and conduct of these trials that are required for approval. Phase 1 trials, conducted by industry, evaluate safety in small numbers of healthy volunteers. Phase 2 trials, often conducted by academicians on larger groups of patients and volunteers, assess dosing requirements and efficacy, as well as safety. Phase 3 trials, often conducted in hundreds or thousands of patients, provide the broader assessment of safety and efficacy for approval.²,³
Step 5.
Submit for regulatory approval

Regulatory agencies oversee the process of drug development and clinical testing. Regulatory oversight continues for as long as the drug is marketed. They evaluate preclinical data to help ensure safe testing in humans, and they approve clinical trial designs. They also evaluate the results to determine whether the therapy is indeed adequately safe and efficacious to warrant approval for marketing.

A pharmaceutical company’s regulatory affairs group works with its clinical divisions to prepare submissions and communicate with the FDA to ensure that studies and data are compliant with all requirements. Data from human clinical trials, some of which are conducted in academic medical centers, are collected and analyzed and used to support the new drug application.

Step 6.
Manufacture a viable therapeutic entity

Manufacturing the therapy can be an expensive, labor-intensive, and high-tech process that is designed to ensure the availability of a safe and adequate supply while maintaining high quality standards on a large-scale basis. It is also a dynamic process with ongoing efforts to increase purity, enhance stability, decrease cost, and reduce the impact on the environment.

Step 7.
Bringing the therapy to patients

After as many as 14 years of research and development, a therapy, if approved by the FDA, is ready to be brought to market. The therapy must be distributed to meet the needs of doctors and patients, while protecting a complex supply chain from counterfeit and contaminated drugs.

Industry also has a responsibility to communicate to and educate doctors and patients about the appropriate use of the medicine, its risks, and its benefits.

Sales visits, industry-supported publications, support lines for physicians, and direct-to-consumer (DTC) advertising all support appropriate use. Visits by sales representatives to introduce a new therapy provide key medical information about its appropriate role, including its indications, side effects, dosing, and access. Later on, representatives may present information from new clinical studies that helps physicians understand a medicine’s evolving role as new data become known. They may also discuss a medicine in the context of published treatment guidelines, which also change over time. DTC advertising...
serves to promote disease awareness and educate large numbers of people about new treatment options and their risks and benefits. Dissemination of advertising and promotion is controlled by FDA regulations.\textsuperscript{3,4}

Studies published in peer-reviewed journals and independently produced educational initiatives contribute to raising the general level of medical knowledge.

**Does academia have a role?**

Teachers and practitioners from academia also play an important role in debating the appropriate use of a new therapy and helping clinicians understand how it ought to be integrated into their practice.

Together, members of industry and academia serve on advisory boards, help interpret safety data, design new studies, and take part in investigator-initiated research.

The education of health care professionals — by both industry and by academia — plays an important role in increasing awareness of new therapies and their role in relation to best practices.\textsuperscript{4,6}

**Monitor for safety**

Safety is monitored and assessed at every point during the drug development process. Potential candidates are screened for predicted safety issues, and then, during preclinical development, they must meet established safety guidelines before they can be tested in human subjects. Clinical evidence is further analyzed and evaluated for potential safety issues during each phase of testing and, for many large, multicenter trials, is continuously reviewed by independent drug safety monitoring boards (DSMBs). Once an application is submitted for approval, regulatory agencies evaluate and review data to help ensure that marketed products have an acceptable safety profile.

Industry is responsible for identifying, analyzing, and reporting to regulatory agencies potential safety issues throughout the entire process of drug development, post-launch, and for as long as the drug is prescribed by physicians.
Advances in HIV treatment have delayed the onset of AIDS and increased life expectancy.

Tremendous strides from “no therapy” to “monotherapy” to “combination therapy” to “personalized medicine” have significantly changed the course of the disease. HIV is no longer thought of as a death sentence, but as a manageable condition. The story of HIV and the therapies used to treat this disease clearly show how industry’s ingenuity in translation of academic basic science research can lead to the development of new therapies that ultimately advance the state of care.

Isolation and culturing of HIV in laboratories made it possible to create antibodies against it. This work enabled the development of diagnostic tests to detect antibodies in response to the virus. As a result, blood supplies could be screened prior to transfusion, and patients could find out if they were infected with HIV before they developed symptoms.

**Translation of scientific discoveries has prolonged the survival of patients with AIDS**

Identification of important genes or segments of genetic material that served as templates for protein molecules within the HIV genome led to the identification of potential targets for intervention. Most advances in the treatment of HIV are the result of drugs developed to inhibit the activity of any of 3 viral enzymes (reverse transcriptase, integrase, and protease) that are essential to viral replication.

In recent years, new drug classes, including entry inhibitors have been discovered that allow drug therapy to be tailored to the individual.

Six years after the identification of Kaposi’s sarcoma and *Pneumocystis carinii* pneumonia, AIDS became a treatable disease with the discovery of nucleoside reverse transcriptase inhibitors (NRTIs). These drugs suppress the replication of retroviruses by inhibiting the enzyme reverse transcriptase.

The discovery of non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors increased the arsenal of therapies used to combat HIV. NNRTIs inhibit reverse transcriptase and prevent conversion of viral RNA to viral DNA. NNRTIs work faster than NRTIs because they are activated once inside the bloodstream. Protease inhibitors inhibit viral replication.
by inhibiting the enzyme protease and aim to prevent an already infected cell from producing more strands of HIV. Until the discovery of protease inhibitors, therapies attempted to prevent infection of a host cell.¹

Advances in the understanding of how HIV functions, the recognition that huge amounts of viral replication continue throughout the entire period of infection, and an increased understanding of the process of developing resistance made it clear that monotherapy had limited usefulness. An increase in the number of different classes of antiviral therapy allowed for a shift to combination therapy and a phenomenon known as pharmacokinetic boosting.⁸

With combination drug therapies known as highly active antiretroviral therapy (HAART), it became possible to reduce the viral load to undetectable levels; however, treatment failures and toxicity issues continued to point to the need for newer therapies. Later on, fixed-dose combinations helped to decrease the pill burden and reduce toxicity.²

Today, therapy for HIV can be matched to the patient to help prolong life

Personalized medicine means the customization of therapy with greater specificity to improve treatment outcomes by matching the correct drug to the patient based on a variety of factors, sometimes including genetics. This kind of customized therapy is yet another strategy to slow HIV progression in patients who have developed resistance to currently available medications.

As a result of the tremendous strides made in the treatment of HIV, AIDS deaths in the US decreased in 1997 by more than 40% for the first time since the isolation of the HIV retrovirus.² Advances made since 1996 in antiretroviral medicines used to treat HIV have extended life by 24 years with a resulting decline in deaths due to AIDS worldwide.⁷
Case history: Alzheimer’s disease

More than 60 years passed from the time that Alzheimer’s disease (AD) was first described to the time it emerged as an area of scientific interest. In the 1960s, the theory that plaques and tangles cause cognitive decline and neuronal death led medical scientists to recognize AD as a disease and not a normal part of aging.

In the mid 1970s, reports that deficits in the enzyme responsible for the synthesis of acetylcholine and confirmation that substantial presynaptic cholinergic deficit along with an understanding of the emerging role of acetylcholine in memory led to the cholinergic hypothesis. This hypothesis led to the approval of the first cholinesterase inhibitor in the early 1990s. However, this agent was associated with severe side effects, including liver toxicity, and is rarely prescribed.

The search for an agent with an improved safety profile led to the discovery of other drugs in the same class that have the advantage of improved tolerability and a decreased incidence of side effects. Later, the hypothesis that continuous activation of glutamate NMDA receptors leads to neuronal damage resulted in the development of an NMDA receptor antagonist.

The limitations of existing therapies for the treatment of AD are a sign of the difficult scientific and clinical challenges facing academia and industry. At present, there are only a few approved treatments, and while these have some benefit, it is imperative to advance research that will expand our understanding of the biology of the disease.

Academic discoveries suggest new targets for intervention that may lead to new therapies

Current treatment focuses on several issues, including managing cognitive and behavioral symptoms and slowing or delaying the disease process. However, the discovery of a genetic link and technological advances in imaging indicate that changes may exist in the brain long before a person develops symptoms of AD. These discoveries are opening the door to new research and the potential for therapies that may prevent, delay, reverse, or halt the nerve cell damage associated with the disease.
While it is clear that more work is needed to understand the biology of the disease, it is hoped that this research will ultimately result in the development of new therapies for treatment and prevention. Some of the many avenues of research that are being pursued include anti-amyloid strategies, such as beta-secretase inhibitors, gamma-secretase inhibitors, statins, and immunization to prevent formation and increase degradation of amyloid. Other therapies, such as tau kinase inhibitors, phosphodiesterase inhibitors, anti-inflammatory agents, tau aggregation inhibitors, and H3 antagonists, are also being researched.9

Collaborations increase the understanding of AD which may lead to more effective therapies

One example of collaboration between industry, academia, and government is the Alzheimer’s Disease Neuroimaging Initiative (ADNI). The goal of ADNI is to define the rate of progression of mild cognitive impairment and AD, to develop improved methods for clinical trials, and to provide a large database, which will improve the design of treatment trials. This project should provide information and methods to improve the treatment of AD and perhaps lead to effective methods of prevention.10 An initiative such as this is only possible with the help of each constituent. Data collected from trials are provided online and in real time, allowing for enhanced access and increased transparency.10

Another example of collaboration designed to facilitate the development and implementation of new treatments is the Alzheimer’s Association research roundtable. This consortium of association staff, scientists from industry, thought leaders from academia, and representatives from government agencies is actively addressing the obstacles to Alzheimer’s research and development, clinical care, and public health education.11

With collaborations such as these, we are moving in the right direction, but more efforts are still needed.
In the early 1900s, a diagnosis of breast cancer meant the removal of the breast and ovaries. It wasn’t until the structure of DNA was elucidated in 1953 that scientists finally understood how mutations in genes could contribute to the development of cancer. Since the early 1990s, treatment has evolved from only invasive surgical options to include less invasive modalities such as chemotherapy and targeted therapy. And, whereas earlier therapies killed all rapidly dividing cells, newer targeted therapies more selectively attack particular components of tumors and cancer cells.

Translation of academic discoveries allowed for the development of therapies with greater efficacy and specificity. Establishment of the links between estrogen and breast cancer and the identification of estrogen receptors were scientific breakthroughs. Translation of this discovery enabled the development of two classes of therapy: selective estrogen receptor modulators (SERMs), which block estrogen receptors, and aromatase inhibitors (AIs), which block the conversion of androgens to estrogens by peripheral aromatase.

Isolation of oncogenes and tumor suppressor genes; identification of tumor targets, such as the human epidermal growth factor 2 (HER2) receptor; and the discovery of angiogenesis increased our understanding of the biology of cancer cells. These discoveries allowed for the development of new kinds of therapies that mimic some of the natural signals that the body uses to regulate growth. These include therapies that specifically inhibit oncogenes or restore normal tumor suppressor gene functions, along with monoclonal antibodies and tyrosine kinase inhibitors that specifically target chemical components of cancer cells. Unlike chemotherapy, which kills both cancer and normal cells, many targeted agents work by affecting the biology of cancer cells, which may or may not

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**Case History: Breast cancer**

Academia and industry collaborating to expand therapeutic options for breast cancer
result in the death of normal cells. The discovery of angiogenesis, the process of forming new blood vessels that allow tumors to grow, led to the development of angiogenesis inhibitors. Other types of targeted therapy can be matched to specific patient populations and have created the opportunity for treating cancer with greater efficacy and specificity than was possible with earlier therapies.

Scientific advances allow for customization of treatment via a multipronged approach

Breast cancer is not a homogeneous disease, and optimal treatment varies from patient to patient. To this end, molecular and genetic advances have allowed for customization of therapeutic options, which may lead to improved outcomes. The identification of breast cancer genes (BRCA1 and BRCA2) has helped to identify women at increased risk for the disease, while genetic profiling has aided risk assessment and helped to predict response to therapy. One example is a test that identifies women with an inherited deficiency in the CYP2D6 gene, which codes for an enzyme that metabolizes tamoxifen into its active metabolites. This test can identify patients for whom tamoxifen is likely to be ineffective so that they can be offered other therapies. These advances, along with the availability of therapies with multiple mechanisms of action, have allowed for treatment to be tailored to the individual patient.

In oncology, collaboration has improved therapies

Over the years, ongoing collaborative efforts have resulted in therapies that improved survival, decreased toxicity and improved tolerability. Recently, academia, industry, and government have come together to develop cooperative groups, such as the The Eastern Cooperative Oncology Group (ECOG), which has provided data that led to a new standard of care for the treatment of breast cancer. These improvements along with a greater understanding of cancer biology have helped move breast cancer from a disease with a poor prognosis and minimal treatment options to one with improved survival with a broader array of available treatments.
The development of vaccines can be traced back to as early as 1796. When Edward Jenner observed that milkmaids who caught the cowpox virus did not get smallpox, he realized that inoculation with one disease (cowpox) resulted in immunity to another disease (smallpox). This theory, that inoculation with a specific pathogen prior to infection may prevent occurrence of a disease, led to the development of therapeutic interventions that can be used clinically and formed the basis of the discovery of subsequent vaccines.

By applying a similar concept, Louis Pasteur improved on Jenner's method and was able to weaken infectious bacteria to create a vaccine and inject it to build immunity. Immunization is the process of injecting a vaccine to stimulate the immune system to build immunity against a particular pathogen. Using this process, Pasteur was able to prevent chicken cholera, anthrax, swine erysipelas, and rabies. Vaccines for plague, cholera, typhoid, diphtheria, pertussis, tuberculosis, measles, and tetanus were also developed.

The collaboration of academia, industry, and government has resulted in the development of vaccines that have decreased morbidity and mortality. Academia provides the basis for translation of research into the development of vaccines by identifying the causative mechanism or agent that leads to disease. Industry then builds upon this research, developing vaccines that modify the disease process or prevent the pathogen or causative agent from causing disease. Advances made in vaccine technology resulted in the creation of conjugate vaccines, live vector vaccines, new adjuvants, genome-based proteomic vaccines, and DNA vaccines and recombinant strains.

Government plays an integral role in the development of vaccines. It provides funding for research, identifies outbreaks, and conducts research on viral strains and test vaccines. The Centers for Disease Control and Prevention (CDC), which was initially formed to address malaria control participated in global eradication efforts for smallpox and control efforts for Legionnaires’ disease, HIV, tuberculosis, and emerging infectious diseases.
Smallpox has been eradicated worldwide. Polio, measles, and rubella have been eliminated in the US, where disease rates from vaccine-preventable diseases since the introduction of vaccines have been reduced by 99%. Vaccines have saved more lives than any surgical technique or medication, including antibiotics, and have prevented 9 million deaths worldwide each year.

Continued collaboration is extending the use of vaccines to other conditions.

Applying a similar concept — that inoculation with a pathogen prior to infection may provide immunity against disease — has resulted in the development and approval of vaccines to treat various conditions that can lead to cancer. For example, vaccines for human papillomavirus (HPV) and hepatitis B virus (HBV) have been approved with the aim of preventing cervical cancer and liver cancer, respectively.

Other promising vaccines in development include those to fight autoimmune diseases, gastric ulcers, rheumatic heart disease resulting from Group A streptococcal infection, and Alzheimer’s disease. Trials of vaccines to prevent HIV infection, several types of meningitis, and pneumonia are ongoing. Developments may one day provide immunologic protection against noninfectious conditions, such as asthma, multiple sclerosis, and diabetes.

The emergence of resistant strains and the growing threat of infectious diseases, such as tuberculosis and typhoid, that were previously controlled but are no longer susceptible to standard antimicrobial therapy and the occurrence of new diseases, such as West Nile virus and severe acute respiratory syndrome (SARS), increase the urgency of collaborating to discover new vaccines.
Industry is about more than profit

After a therapy has been approved, industry supports its safe and effective use through a wide range of activities. Sales representatives and journal advertising inform physicians about its availability and appropriate use, and direct-to-consumer (DTC) advertising informs consumers about the availability of the new treatment option. Without these activities, the ability to apply therapeutic advances to everyday practice in a timely manner would be very limited.

“There is a clear need for interactions between physicians and the pharmaceutical industry to ensure the free flow of valid scientific information. When the information is accurate and complete, physicians have the necessary tools to make the right prescribing decisions.”

American Medical Association

Communication helps translate research findings into clinical practice and personal behaviors

Gaps in care suggest that new therapies do not enter into practice based solely on clinical evidence alone. For example, in 1981, the Beta-blocker Heart Attack Trial established the benefits of beta-blocker therapy in patients recovering from a heart attack, yet 15 years later, beta-blockers were being prescribed for only 63% of these patients. According to the Institute of Medicine, it takes up to 17 years to incorporate just 30% of clinical recommendations into practice. That may explain why many conditions remain underdiagnosed and undertreated. A 2003 study by RAND Health showed that patients in the US receive about half of recommended care, and about a third of the time, patients fail to receive medication according to quality standards. Industry’s marketing and promotional activities, while serving to promote their products, also raise physician awareness of advances in clinical practice and encourage patients to get the treatment they need.

Promotional activities provide evidence for informed decisions

When manufacturers provide information on new treatment options, clinical support, dosing information, and updates on safety and risk, they give physicians the information they need to make independent treatment decisions. A 2008 KRC Research survey of physicians showed that 95% of them valued information from representatives about the latest drugs and treatments.

A majority of physicians find information from pharmaceutical companies useful and reliable

Improved physician/patient dialogue helps diagnose diseases that might otherwise be untreated or undertreated

Today, patients are seeking more information about diseases and treatments, asking questions, and making decisions regarding their health care. Dissemination of information to consumers about diseases and available treatment options enables patients to become more engaged in their own care.

In 2006, a consumer survey found that DTC ads resulted in 56 million Americans talking to their doctors. Diseases and conditions that might otherwise remain undiagnosed, untreated, or undertreated are now more openly discussed. A 2007 KRC Research survey found that 1 in 4 consumers sought medical advice after reading a DTC ad, while 4 in 5 consumers agreed that prescription drug advertising educates them about health conditions and treatment options.

A survey of 500 physicians conducted in 2002 by the FDA about DTC advertising found that 73% believed it helped patients ask thoughtful questions regarding their health and more than half thought it improved the discussions they had with their patients.
A company’s medical organization supports the appropriate use of a product
Following the introduction of a product, the medical organization continues to provide medical information, performs clinical trials that expand the knowledge base, performs pharmacovigilance assessments, and reviews all promotional material for medical accuracy. Medical liaisons maintain an open channel of communication with the medical community and support research. Medical information services answer inquiries and respond to requests for medical and scientific information. These communications support the medical community and their ability to safely and effectively use a therapy once it has been introduced.

Promotional materials are strictly regulated
Pharmaceutical companies have regulatory, legal, and medical reviews in place to ensure the accuracy, fair balance, and compliance of all promotional materials with FDA mandates. Statements made about products must be accurate, truthful, and nonmisleading. They must also be properly substantiated, reflecting a balance between risks and benefits, and must be consistent with the label and all other FDA requirements. Prior to a new drug’s launch, promotional materials are reviewed by the FDA and the materials continue to be submitted to the FDA after its introduction.

Industry funds most biopharmaceutical research
Science, research, and technological development of new therapies require significant investments of time and money. Without the profits from successful therapies, the amount of capital available to fund future cycles of R&D could be reduced by two thirds.

In 2006, industry funded 60% of the $73 billion spent on biopharmaceutical research in the US

R&D investment from US biopharmaceutical companies increased from $2 billion in 1980 to $65.2 billion in 2008. Among members of the Pharmaceutical Research Manufacturers Association (PhRMA), the annual domestic R&D investment of $38 billion in 2008 far exceeded the total value of promotional expenditures.

Spending by PhRMA member companies on domestic R&D in 2008 compared with spending on promotional activities

![Bar chart showing spending on R&D, Detailing, DTC Advertising, Meetings and Events, Journal Advertising, and Marketing]

- R&D: $12 billion
- Detailing: $4.7 billion
- DTC Advertising: $3.4 billion
- Meetings and Events: $0.4 billion
- Marketing: ($20.5 billion)

*Does not include the cost of free samples provided to physicians
†Adapted from PhRMA Pharmaceutical Industry Profile 2009.
‡Adapted from Congressional Budget Office, 2009.

The number and types of clinical trials being conducted are important indicators of R&D performance. In 2008, 21,795 clinical trials were active in the US.

Active US Clinical Trials for Selected Conditions in 2008

<table>
<thead>
<tr>
<th>Selected Conditions</th>
<th>Numbers of trials</th>
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<tr>
<td>Cancers and Other Neoplasms</td>
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<tr>
<td>Rare Diseases</td>
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<td>Behavioral and Mental Disorders</td>
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<td>Alzheimer’s Disease</td>
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</tr>
</tbody>
</table>

Adapted from Burns LR, 2009.

*PhRMA is an organization that represents the leading research-based pharmaceutical and biotechnology companies in the US.
Committed to addressing the issues

Safety

Perception:
Drugs are marketed before they have demonstrated adequate safety

All drugs have side effects; the severity and type depend largely on a drug’s mechanism of action. Because all drugs have the potential for adverse reactions, risk must be weighed against the potential benefits of their intended use.

In the research and development phases, an important objective is to screen out molecules with anticipated safety issues. Preclinical testing is then conducted in vitro and in vivo to further evaluate the safety and potential efficacy of a therapy. Only after an acceptable safety profile has been established through screening and animal testing, does a therapy advance to clinical testing in humans – first in small trials (Phase I) to evaluate safety, and later in larger trials (Phase II and III) that assess safety and efficacy.1

While signals revealed in the data from these trials may point to potential safety issues, these are weighed against the potential benefit.1

Even with rigorous testing in the thousands of individuals who participate in large trials, there is still the possibility of low-frequency safety issues that may be revealed only after the drug has been taken by millions. After a drug is launched, its safety is monitored by both the company and the FDA.1 And as long as a drug is prescribed by physicians, pharmaceutical companies – with FDA oversight – are responsible for identifying, analyzing, and reporting to regulatory agencies all significant events that could indicate a safety issue. If unanticipated and severe side effects do occur, companies work with the FDA to determine the best course of action, which may include updating the labeling, issuing safety alerts, or withdrawing the therapy from the market.2

Although there is no such thing as absolute safety, the goal is the development of therapies that advance patient care with acceptable risks. To this end, safety is monitored and managed at every point during the drug development process and beyond.1

Development of “me-too” drugs

Perception:
Industry is only interested in developing profitable “me-too” drugs with little benefit

There are actually several reasons why this argument is not as compelling as it sounds.

First, competing pharmaceutical companies may work in parallel on targeting a pathway or addressing a therapeutic need, resulting in approval of similar drugs at about the same time. So, in many cases, me-too drugs are the result of parallel development rather than imitation.2 Because development is a lengthy process lasting up to 14 years with many dead ends and inevitable disappointments, it’s not possible to predict which therapies will be successful. A promising therapy may be tested in thousands of patients before unacceptably high rates of adverse events are revealed, which ends the drug’s development. As a result, a drug that might have been second to market, and seen as a me-too agent, may now be first.

Second, the efficacy and tolerance of a single medicine can vary from person to person. Theoretically, drugs of the same class should have a similar effect in all patients. However, because not all patients are identical, some respond well to one drug but not to others; therefore, other options are necessary for doctors to manage diseases across a heterogeneous population. Different therapies, while similar to others in their class, can also be matched to specific subpopulations, while the ensuing competition can drive down prices.2

Last, the first-in-class drug is not always the best. Therefore subsequent options within the same therapeutic class can offer improvements over the current standard of care. Efforts to improve safety, efficacy, tolerability, specificity, and delivery are continual, and advances in care are usually incremental changes.2
**Perception:**
Scientific integrity of studies and publications is compromised by industry goals

We recognize that there have been failures, but changes have been made to address concerns around transparency in clinical research that is sponsored and conducted by pharmaceutical companies. *Industry strives to maintain the highest ethical and scientific standards.* To this end, all clinical research trial designs are reviewed by an independent ethics committee or Institutional Review Board (IRB) before trials can be conducted. Good Clinical Practice (GCP) guidelines are followed to ensure that ethical standards are observed. *Studies are designed and conducted in accordance with industry, legal, and FDA guidelines.* Research programs are evaluated based on potential benefits and weighed against inherent risks to patients. Clinical investigators review and conduct trials and ensure that the rights of all participants are protected. *Industry strives to provide quality data and accurate scientific information.* For new research, results are collected, analyzed, and reported under the scrutiny of the FDA. The results and significance of these studies are published and discussed in peer-reviewed journals. And, in an effort to increase transparency, results of clinical trials are now being posted on ClinicalTrials.gov and ClinicalStudyResults.org.

**Perception:**
Industry is not interested in developing drugs to treat third-world diseases

While there is some historical validity to this argument, *pharma is now demonstrating a commitment to address global health issues.* The health of people in the developing world is a challenge and a responsibility for everyone. Consider, though, that the success and growth of all businesses, including those that develop medicines, is based on a commercial model. In pharma, profits support R&D, which supports a company’s growth, as well as advances in care. And, while historically, the focus has been on developing therapies for those Western societies that can afford to pay for it, business models today are evolving to help pharma do its share to alleviate the burden of disease worldwide. For example, the launch of Global Health Progress brings industry, world health leaders, and policy makers together in partnership to focus on neglected diseases in developing countries. *Industry-driven commercial business models are being developed that focus on improving access to medications in emerging markets.* Newly created divisions within companies now focus on diseases in the developing world, such as malaria and hepatitis C. In an effort to improve global access, key medications and vaccines are being sold on a “differential” pricing basis to make them more accessible. Recently, companies have offered licenses to manufacturers in the developing world to produce generic versions of their HIV medicines. This approach allows companies to maintain their profitability, while recognizing their responsibility and commitment to improving the health of individuals in the developing world. Industry is also partnering with non-profit and private organizations to meet the global health challenge. *Industry’s philanthropic programs improve access to medicines and health care around the world.* These initiatives have provided more than 77 million treatments for trachoma, 50 million doses of medicine for children with or at high risk for intestinal worms, 1 million injectable doses to fight sleeping sickness, and a donation of $125 million worth of vaccines and medicines to combat a variety of other diseases that occur in third-world countries.
We are not that far apart

We recognize that the world has changed and that many in academia are sensitive to current and past practices. As a result, we have voluntarily changed our marketing practices in an effort to base our interactions on the highest ethical standards focused on the principle that care should be guided by each patient’s medical needs and the knowledge and experience of the physician. We are reinforcing our intentions with a code designed to benefit patients while enhancing the practice of medicine.1 And as you will see below, current marketing practices are actually not that far from those advocated by the Association of American Medical Colleges (AAMC).

Current marketing practices closely aligned with those recommended by AAMC

<table>
<thead>
<tr>
<th>Practice</th>
<th>PhRMA code*1</th>
<th>Degree of alignment</th>
<th>AAMC provisions*2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gifts and leave-behinds</td>
<td>Ban on all except those designed for the education of patients or health care professionals.</td>
<td></td>
<td>Ban on all gifts.</td>
</tr>
<tr>
<td>Consulting practices</td>
<td>Activities should be conducted in full compliance with policies of the medical center. Compensation should reflect fair market value for services provided.</td>
<td></td>
<td>Ensure that consultant arrangements are neither inducements nor rewards for prescribing or recommending a particular medicine or course of treatment. Compensation should be reasonable and based on fair market value.</td>
</tr>
<tr>
<td>Food</td>
<td>Limited to in-office or in-hospital presentations that provide scientific or educational value. Meals should not be directly provided by company at CME programs.</td>
<td></td>
<td>Ban on all food except in connection with ACCME programs.</td>
</tr>
<tr>
<td>Representative access and credentials</td>
<td>Trained and have sufficient general knowledge to provide information consistent with FDA guidelines.</td>
<td></td>
<td>By appointment or invitation and only in non-patient care and public areas.</td>
</tr>
<tr>
<td>Practice</td>
<td>PhRMA code</td>
<td>Degree of alignment</td>
<td>AAMC provisions</td>
</tr>
<tr>
<td>----------------------------------</td>
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</tr>
<tr>
<td>Scholarships and educational funds</td>
<td>Carefully selected educational conferences may be offered. Recipient of funds is determined by the academic institution.</td>
<td>![Circle]</td>
<td>Funding should go to central administration office; selection of recipients is the sole responsibility of the academic medical center.</td>
</tr>
<tr>
<td>CME</td>
<td>Separate CME grant-making functions from sales and marketing departments. Funding should be given to CME provider. Comply with ACCME regulations and policies.</td>
<td>![Circle]</td>
<td>Funding should go to central CME office and programs should comply with ACCME standards.</td>
</tr>
<tr>
<td>Speaker programs</td>
<td>Provide full disclosure of the existence and nature of relationship. Programs are held in venues conducive to informal communication and training.</td>
<td>![Circle]</td>
<td>Discourage participation in industry-sponsored speakers’ bureaus.</td>
</tr>
<tr>
<td>Samples</td>
<td>Appropriate to provide for patient use in accordance with the Prescription Drug Marketing Act.</td>
<td>![Circle]</td>
<td>Samples should be centrally managed or managed to minimize risk of impropriety.</td>
</tr>
<tr>
<td>Interaction with students and residents</td>
<td>For educational purposes only.</td>
<td>![Circle]</td>
<td>For educational purposes and only under the supervision of a faculty member.</td>
</tr>
</tbody>
</table>

*PhRMA is an organization that represents the leading research-based pharmaceutical and biotechnology companies in the US whose mission is to conduct effective advocacy for public policies that encourage discovery of important new medicines for patients by pharmaceutical/biotechnology research companies. Adherence to the PhRMA code is voluntary on a company-by-company basis.*
The progression of research and development: Advancing the state of care

The introduction of new therapies not only improves the state of care, it raises the bar for subsequent discoveries. Unlike earlier therapies, which were compared with placebo or less effective agents, newer development must now meet and exceed the higher standards of safety and efficacy. Each advance creates the potential for improved outcomes, adds therapeutic options, and contributes to the knowledge base.
The reasons to work together are many

**Prevent, slow, or halt the progression of Alzheimer's disease**
In 2008, an estimated 5.2 million Americans of all ages were reported to have Alzheimer's disease.¹ Drugs available on the market today offer modest benefits. More effective therapies that prevent, slow, or halt the progression of the disease are needed.

**Slow progression and reverse the effects of arthritis**
According to annual estimates, 1 in 5 US adults have arthritis.² Current therapies can only manage the pain, but they fail to significantly improve the course of disease. Many patients do not respond to available disease-modifying medications. New therapies to reduce the side effects and reverse the course of disease are needed.

**Prevent, cure, arrest, or delay cancer**
Over 7 million people died of cancer in 2004, and if current trends continue, 83 million more will die by 2015.³⁴ Advances in tumor knowledge and the development of targeted therapies have delayed progression, improved survival, and palliated symptoms, but often with adverse effects. Newer, more effective, and less toxic therapies that prevent, cure, arrest, or delay the progression of the many different types of cancer are needed.

**Prevent or treat cardiovascular disease**
Cardiovascular disease is the major cause of death in the US.⁵ Even with the availability of effective therapies for some conditions, a huge unmet need exists for novel therapies that prevent or treat heart failure, cardiomyopathy, and ischemic heart disease.

**Prevent or treat diabetes**
Diabetes now affects nearly 24 million people in the US.⁶ Although existing drugs can be effective in achieving glycemic goals, none induce weight loss in obese patients. Therapies that lower blood glucose while promoting weight loss and that slow the progression of disease are needed.⁷

**Prevent or cure HIV**
The number of people living with HIV worldwide in 2007 was estimated at 33 million.⁸ Existing treatments have delayed the onset of AIDS and increased life expectancy, but none have been able to prevent or cure the disease. Therapies that prevent the transmission of the virus or that cure the disease in infected individuals are needed.

**Prevent and treat malaria**
Each year 350 to 500 million cases of malaria occur worldwide, and over 1 million people die, most of them young children in sub-Saharan Africa.⁹ Therapies for malaria in developing countries are needed to combat the development of drug resistance, prevent the spread of malaria, and treat those infected.

**Improve control of pain**
An estimated 50 million Americans live with chronic pain.¹⁰ While newer therapies are more effective at controlling pain, inadequate pain control, and side effects associated with increased dosing necessitate the need for safer therapies with fewer side effects.

**Improve reduction of obesity**
Obesity is a major risk factor contributing to many serious cardiometabolic disorders.¹¹ The financial burden of obesity and its associated conditions is huge. Diet and exercise are the preferred methods for losing weight, but are associated with high long-term failure rates.¹² Current therapies have limited long-term impact. More effective long-term therapies with fewer side effects are needed.

**Prevent progression of Parkinson's disease**
Parkinson's disease affects about 1 million people in the US and 4 million worldwide.¹³ Current therapies help manage symptoms, but none stop or prevent the progression of the disease. Neuroprotective therapies that can prevent or stop the progression of the disease or restore cognitive function are needed.