BY DENISE MYSHKO

# CROSS-FUNCTIONAL TEAMS
# Models of Success

Representation from all the key disciplines — **toxicology, pharmacovigilance, clinical research, pharmacology, manufacturing, legal, and, yes, marketing** — is essential for drug-development success today. A cross-functional model allows companies to bridge the gap between R&D and commercialization to bring products to market quicker and more efficiently.

**PharmaVOICE interviewed four cross-functional teams for this month's Forum. Representatives from MedImmune, Wyeth, Novartis, and Kalypsys** provide insights into what makes multidisciplinary teams successful.

A multidisciplinary-team approach that bridges the gap between R&D and commercialization silos may be one of the most difficult business models to employ within pharmaceutical drug development.

The structure, in and of itself, is rife with pitfalls: inadequate resource allocation — budgetary and personnel — geographic divides, stakeholder participation, senior management buy-in, and so on. But if organized with thoughtful consideration and proper training, a cross-functional team can improve the path to market.

Within a cross-functional team environment, decisions are made in a more timely fashion, efficiencies are gained through iteration, and expertise is focused around a therapeutic area — all of which can lead to bringing products to market quicker and more efficiently.

Many analysts believe that the era of the "big pharma model" has outlived its usefulness. While this may or may not prove to be an accurate prediction, the participants in this month's Forum, many of whom belong to "big pharma" organizations, recognize that there is a need to change the current paradigm.

At the recent Drug Information Association meeting in Philadelphia (see related coverage on page 70), Wyeth Research's Charles T. Gombar, Ph.D., VP of project management, outlined why new approaches to clinical development are necessary. Wyeth recognized that the current model for drug development is not sustainable, and as such the company has implemented a series of long-term business initiatives to improve its processes, based on industrywide business and scientific drivers as well as company-specific drivers (see page 16 to read about Wyeth's cross-functional model approach).

Dr. Gombar identified spiraling R&D costs, increasing cycle times, rising attrition, and poor value definition as a few of the industrywide business drivers. When it comes to the science, he outlined the need to increase innovation, complexity of disease, and new technologies and approaches as some of the industrywide drivers that all companies should be evaluating.

As one of our thought-leaders rightly points out, there are no hard and fast rules for when companies should form a multifunctional or cross-functional project team, but the

consensus is, the earlier the better. As team leaders, program managers, and functional directors know each team is unique, so it's important that the teams are developed around specific skill sets and areas of expertise.

Our Forum experts and industry thought leaders (see box on page 26) agree: the end result is to bring products to market that meet unfulfilled patient needs.

The Tufts Center for the Study of Drug Development is hosting a program this October on the topic of leadership for drug-development teams and how to improve cross-functional R&D performance. Part of the curriculum during the three-day course addresses the techniques that leaders need to field a successful cross-functional team, such as:

• Motivate team members — Engage people from diverse organizations to own the plan and commit to milestones.

• Manage up — Enroll senior executives in supporting your team and removing roadblocks.

• Bridge boundaries — Communicate productively across functional silos, geographic divides, cultural barriers, and company borders.

• Align toward shared goals — Build collaboration among team members with disparate perspectives and priorities.

• Move difficult conversations forward — Reframe controversial issues to enlist the team in making progress.

• Maintain momentum in the face of change — Achieve project goals in a dynamic environment of M&A, new alliances, changing processes, and restructured organizations.

## Best Practices for **Cross-Functional Team Success**

**In its ongoing efforts to enhance its range of drug-development services for its customers, INC Research has developed a series of best practices that address optimal cross-functional team success.**

- Clearly define expectations across all project team members — sponsor, CRO, vendors — that address providing quality deliverables on time and on budget.
- Develop effective, consistent communications with visibility on the overall project.
- Engage therapeutic expertise leading to knowledge, foresight, and predictability of results.

Taking into account these critical factors for success, INC Research developed a three-part, repeatable process (called Trusted Process) that enables project teams to meet stated expectations and requirements.

The first of INC Research's processes is called QuickStart, which enables the rapid movement of a project through the initial phases of a study. It starts with goal alignment at pre-award through the start up and into the enrollment phase. The project team has a sense of urgency to move the start-up process as far as possible toward first patient enrolled as its goal.

The next step is a kick-off meeting attended by key decision makers and core project team members from the sponsor and third-party suppliers, as appropriate. This kick-off meeting creates a shared vision on how to: conduct the study; define roles and responsibilities; discuss challenges, timelines, and deliverables; and validate assumptions made during the proposal stage. At this point, a customized communication plan is drafted, including objectives, team charter, and a defined decision escalation path to ensure effective communications throughout the life of the study.

The next step involves an intensive work session, in which core team members develop, review, and approve start-up documents and risk-management plans and make key decisions to rapidly move the project from start up into the enrollment phase.

The project team then returns to its regular work environment with a sense of accomplishment as it relates to team dynamics and start-up deliverables. The members are focused on enrollment, quality excellence, and the execution of approved project plans.

**Gaining feedback from the project teams is critical to capture the benefits and opportunities for success. Some common areas that should be tracked include:**

- Roles and responsibilities
- Alignment of the entire team to project goals and expectations
- Cycle times for start-up activities and documents
- Commitment and project ownership for team members

**"Clearly defined expectations across all project team members — sponsor, CRO, vendors — should address providing quality deliverables on time and on budget.**

Brenda Muldrow
*VP of Customer Relations*
INC Research

Source: INC Research Inc., Raleigh, N.C. For more information, visit increasearch.com.

# MEDIMMUNE
## The Next Level of Decision Making

MedImmune Inc. was awarded a $170 million contract from the U.S. Health and Human Services Department (HHS) to develop cell-based seasonal and pandemic vaccines using its proprietary live, attenuated, needle-free influenza vaccine technology.

One of the reasons that the company won the contract was based on its response to the request for proposal (RFP), which included a team approach for execution that would result in more effective and faster decision making.

The company plans to expand its domestic manufacturing capacity by establishing a cell-based facility in the United States. MedImmune's new facility will be able to produce at least 150 million doses of the vaccine within six months of notification of any influenza pandemic.

MedImmune's influenza vaccine, FluMist, is currently made using chicken eggs, as are all other approved influenza vaccines in the United States.

Delivered as a nasal mist, FluMist is a live virus vaccine that uses a modified attenuated (weakened) form of the influenza virus to stimulate a protective immune response in the body. The vaccine is indicated for healthy people 5 to 49 years of age.

The company's manufacturing process for FluMist requires far fewer eggs than other manufacturers because its vaccine technology has dose yields that can be as much as 100-fold higher than the flu shot.

The company has the capacity to scale up to 45 million bulk doses per month upon development of monovalent pandemic vaccine using egg-based production methods.

By applying a cell-based production capability, MedImmune anticipates having the capacity to produce 300 million to 400 million monovalent doses of a pandemic vaccine annually.

### Meet the **MedImmune Team ...**

**MedImmune Inc., Gaithersburg, Md., is dedicated to advancing science and medicines and is focused on the areas of infectious diseases, cancer, and inflammatory diseases. For more information, visit medimmune.com.**

**GEORGE COX**, Senior Director, Supply Chain, Manufacturing, is responsible for coordinating the operations in the United Kingdom and Pennsylvania. His role on the team was to represent the operations group from a cell-culture manufacturing standpoint.

**GEORGE W. KEMBLE, PH.D.**, VP, R&D, Vaccines, was the principal investigator for the HHS contract. Dr. Kemble acts for the program-management office to coordinate the activities of the various teams.

**MICHAEL MASSARO**, Director, Strategic Operations, acts as a central voice of the clinical-development group. For the pandemic team, he coordinated responses to the RFP on behalf of the clinical-development organization.

**ALAN TAGGART**, Influenza Vaccines Program Manager, is responsible for integrating the different teams in the influenza program and making sure the company tracks with the government contract. He also was responsible for integrating the proposal across different functions.

**NICK TRESSLER**, Manager, Operations Business Support Team, Finance, is responsible for analysis and consolidation of the company's manufacturing plants. His role on the team included putting together the cost proposal and establishing MedImmune as a government contractor.

**LOTA S. ZOTH**, Senior VP and Chief Financial Officer, played a supportive role in the team process in addition to her day-to-day responsibilities.

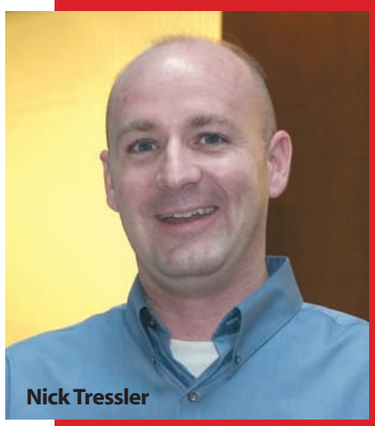
## A Coordinated Effort

*At MedImmune there is a recognition that no one person, or function, or technology can do all the work to get a product out the door. A team approach allows MedImmune to bring all of its functional areas and expertise to the table to successfully execute development programs.*

**ZOTH.** We all know we can't do it by ourselves. We have to collaborate with all of the members of the product-development team. This team approach allows functional areas to bring their individual expertise to the table. We have someone who is designated as the team leader, and the team has certain objectives. As a company, we didn't appreciate this approach until a couple of years ago, and it's really only in the last couple of years that we have started practicing team-structure theories.

**TAGGART.** Because the HHS program is so large and involves several cross-functional teams around major sets of activities, we had to have a single point of oversight. So we put a program-management office in place to coordinate all of the activities on a weekly

Members of MedImmune's multifunctional team responsible for the HHS contract talk about their processes, what made them successful, and what's next for them.


Nick Tressler


Michael Massaro


George Cox


Alan Taggart

> **Michael Massaro**
> The multidisciplinary team was a living organism, which speaks to its flexibility.

basis. I think this works well because we all have a vision of where we want to go. We wanted to develop cell-culture processes within the contract time line, which is within five years of submitting a BLA for the process. We are all working toward that goal. We all understand the intermediate milestones we have to get to, and we're all on the same page.

**TRESSLER.** There was a sense of urgency to win the contract, which is going to fund the development of a new vaccine method. We had a lot of strong executive support, and that makes a difference.

**KEMBLE.** Could this project be done without a multifunctional team? I don't think so. There are many tales of heroic efforts that moved a project program along, but this HHS program is so complex that it could not be done without a multifunctional team.

**MASSARO.** The different line functions knew that collaboration was needed for the team goal of securing the contract. There were no silos or function battles. Everybody understood what the team needed to do to move forward.

**COX.** The team worked very hard to put the proposal together. Many of the people on that team are now responsible for making sure the commitments that were made in the contract are met. Part of this team is developing a methodology to respond to additional requests for information and proposals. We want to demonstrate that MedImmune is a leader in the influenza business.

## Lessons Learned Along the Way

*While an evolving concept at the company, MedImmune's cross-functional team members say the manufacturing contract with the HHS taught them to be flexible and to accommodate changes along the way.*

**ZOTH.** One of the big lessons learned, in terms of fielding a successful team, is to have extremely clear lines of communication, and

> **Alan Taggart**
> There is no one way to develop a high-performing team. We found a way to be successful because we understood the end goals and had the organization behind us.

there has to be a very well-understood decision-making tree.

**MASSARO.** Instituting a structure whereby there was an accountable core group of people, who had a clearly defined task, hit home through out the whole MedImmune organization.

**TAGGART.** Taking the project to the next level involved evaluating how we made decisions, which needed to be done effectively and timely so that the overall project wasn't impacted or slowed down. There were obviously big decisions that the teams needed to make, and sometimes key executives needed to be involved in those decisions. We needed to learn how to facilitate that process so the project could move forward.

**COX.** As we got the team up to speed, people began working more cohesively and cross-functionally to tell a story and demonstrate to the government that MedImmune has significant advantages in the influenza and cell-culture business and that we have capabilities on tap to help with pandemic readiness. We had a team that was absolutely passionate about what it could do.

**TRESSLER.** The team was not only cross-functional, but it had a diversity of levels, including senior executives, directors, and managers. Whoever had the knowledge or information for a particular aspect of the project would assist with team leadership. There was a lot of trust in the team and respect for each person who took the lead on a particular issue.

**ZOTH.** The key to success is how companies execute the team approach. If the team is truly empowered with decision-making capabilities and the organization practices flexibility and allows people to truly bring their expertise to the table, then a multi-functional team can be successful.

## Obstacles Faced

*The hurdles MedImmune overcame revolved around taking the project-management processes to the next level through the use of the team concept.*

**TAGGART.** One of the initial challenges was gaining the credibility throughout the organization that the team had the right make up. We earned that trust by submitting a well-prepared business and technical proposal that was reviewed by the company's senior executives. We also had to find ways to make more expeditious decisions. Maybe it was okay to take a few weeks to make a decision in the past; but we were being held to very specific milestones, and we had to make sure we were hitting those milestones.

**KEMBLE.** The HHS contract was a more complex task than most of us were accustomed to grappling with. Traditionally, if questions arose, they would be pushed back to the appropriate functional area for a solution. When we started with the HHS project, we struggled with the process of how to get the right information within the team structure to arrive at a solution. Now, there is a much better communications structure, and even people who are not directly on the team have opportunities to have their ideas heard.

**MASSARO.** We were used to be being the "sponsor," where we identified the vendors to help us complete our projects. In this instance, we became the vendor, and that was a fundamental change in how we went about responding to challenges. Once we started to think of ourselves as a CRO, of sorts, we were in a better frame of mind to respond to the sponsor's needs and requests, which in this case is the HHS.

> **Nick Tressler**
> The team involved more functions outside of R&D and was much more integrated than typical teams. Now that we have developed a process, we will be able to replicate this model in the future.

## Accomplishments and Successes

*The MedImmune team attributes its success to the common vision the team members had: getting the HHS contract.*

**KEMBLE.** We're trying to take a very complicated set of tasks that are inter-related and put them together.

**TRESSLER.** Our success in getting this contract can be attributed to three things. No. 1 was our unique technology. No. 2 was this team. And No. 3 was our ability to be compliant with all aspects of the government contract.

> **George Cox**
> Projects often have only one bandleader at a time. We had five or six who were able to get the orchestra playing together, which is typically pretty hard to do.

**MASSARO.** I believe MedImmune has a superior product and technology that we, as a company, can leverage to have a direct health benefit. And it was incumbent on us to tell that story to the HHS. The way that we pulled this team together and told our story was the real accomplishment. And part of any effort involves ensuring buy-in from the top levels of the organization, which we had. With buy-in from the executive level, these types of projects can succeed. Absent of that, it's all window dressing.

**KEMBLE.** There was a lot of very important work that had to be done in a very short time frame. The program stretched a lot of people, and it certainly stretched the organization. In retrospect, the contract was a great event that enabled a lot of things to happen. I think, as a company, we've come out the other side much stronger than we had been.

**TRESSLER.** The team involved more functions outside of R&D and was much more integrated than typical teams. Now that we have developed a process, we will be able to replicate this model in the future. ✦

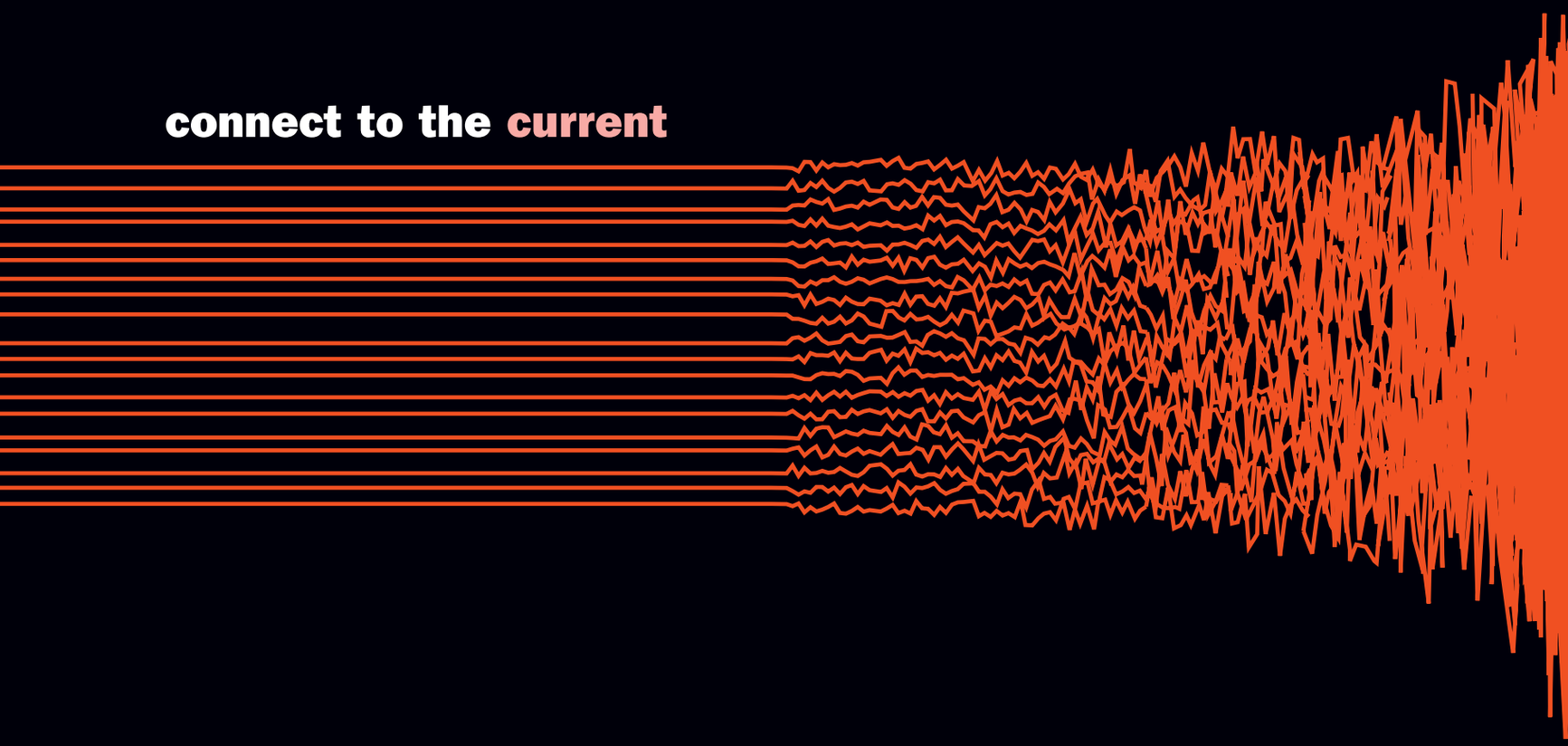
# World-class brands.

**GARDASIL®**
[Quadrivalent Human Papillomavirus
(Types 6, 11, 16, 18) Recombinant Vaccine]

**SINGULAIR®**
(montelukast sodium)

**ZOSTAVAX®**
[Zoster Vaccine Live (Oka/Merck)]

## connect to the current



A world-class experience
for your global brands
connect@juicepharma.com

JUICE
PHARMA ADVERTISING

Tablet-PC ready

# WYETH
## Learn and Confirm

Wyeth is constantly adapting and changing to meet the demands of the market. Recently the company launched a new initiative, known as the Wyeth Clinical Development Model of the Future. Initially, the effort focused on idea generation to enrich and maximize the efficiency of clinical development. Company management conducted more than 60 internal interviews with Wyeth executives and managers; 12 cross-industry case interviews (e.g., Dell, UPS, and Lockheed); and meetings with senior FDA personnel.

At the end of the process, the company adopted a "Learn and Confirm" model, which is a two-stage approach adapted from a model first proposed in the late 1990s by University of California San Francisco Professor Lewis B. Sheiner.

Wyeth's Learn phase is a new way of accomplishing the traditional Phase I and Phase II approach. The goal is to optimize the understanding of a new drug candidate to maximize its medical value and determine if it justifies continued investment. During the Learn phase, Wyeth determines if a candidate drug can be used in representative patients based on acceptable benefit/risk ratio by examining the relationship between prognostic variables, biomarkers, dosages, and outcomes.

The Confirm phase encompasses the traditional Phase III requirements. At this stage, the company focuses on speed and cost-effective confirmation of the drug's safety, efficacy, and value for successful registration and market launch. To move to the Confirm stage of advanced clinical development, compounds must meet specific deliverables, for example clinical activity, drug metabolism, safety and tolerability, dosage and administration, as well as operational feasibility. The goal of the Confirm phase is to demonstrate, in a large and representative patient population, that an acceptable benefit/risk ratio has been achieved. Wyeth has vetted its new Learn and Confirm model with regulatory agencies and has received very positive feedback.

As part of this effort, the company has revamped how its teams are organized. Now Wyeth has core teams with about eight to 10 individuals representing some of the key disciplines, such as regulatory affairs, commercial, manufacturing, chemical development, and formulation development.

One of these core teams is working on ERB-041, a new molecular entity in development for inflammation for rheumatoid arthritis and endometriosis. It's currently in the Learn phase (Phase II). Several members of this development team spoke with PharmaVOICE about the project and the opportunities this new team structure creates for Wyeth.

### Meet the **Wyeth Team ...**

**Wyeth Research, Collegeville, Pa., is one of the world's largest research-driven pharmaceutical and healthcare products companies. For more information, visit wyeth.com.**

**DAMON L. BASS D.O., FACR**, is Associate Director, Inflammation, Clinical Research & Development. In addition, he functions as a medical monitor for one of the company's clinical trials.

**F. OWEN FIELDS, PH.D.**, is Director II, Global Regulatory Affairs. He serves on this team, as well as other teams, to advise of regulatory requirements applying to the specific drug.

**WILLIAM JACOBSON, PH.D.**, is Director, Project Management, Women's Health & Pharma Business Units. He leads a number of cross-functional teams and, as the team leader, acts to coordinate the team and ensure the multifunctional team members are aligned. As part of his responsibilities, he oversees two subteams that are working on the same molecule in different therapeutic areas.

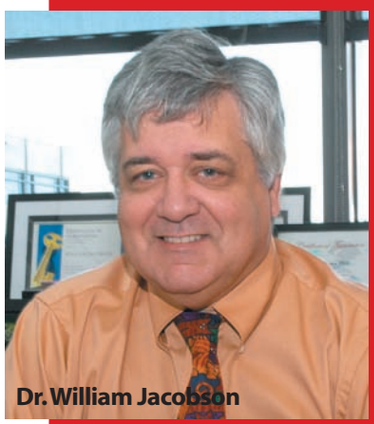
**ROBERT H. MICHEL** is Director, New Products, Women's Health Care. His role on the team is to represent the commercial aspects of the development of ERB-041 for endometriosis.

## The Team Structure

*With so many disciplines involved in drug development, Wyeth managers say a team structure is imperative for maximizing efficiency.*

**JACOBSON.** Drug development in itself is multidisciplinary. A company can't develop a drug simply with people who have clinical expertise or particular medical expertise. We have to discover the drug. We have to learn as much as we can about it. We have to learn how the body handles it, how it is distributed, how it is metabolized, how it's excreted. We have to learn how to formulate the drug, how to present it to patients in such a manner that they have appropriate exposure to the drug. All of these things have to be considered. We have to be able to satisfy all of the regulatory

As part of Wyeth's commitment to "Learn and Confirm," the company has revamped how its teams are organized. In the past, Wyeth had very broad representation on its development teams, with about 25 or 30 people from many different global areas. Now, the company has core teams with about eight to 10 individuals representing some of the key disciplines, such as regulatory affairs, commercial, clinical, manufacturing, chemical development, and formulation development.



Dr. William Jacobson

Dr. Damon L. Bass

Robert H. Michel

Dr. F. Owen Fields

requirements. We need to understand the commercial value of the product, to understand the unmet medical need, what the market is looking for so that we are developing products that truly are needed. We certainly need to understand how we're going to study the drug chemically. Once we decide how we're going to study it, we have to implement the plan. We have to have the appropriate patent coverage. We need to assess intellectual property to make sure that we are not infringing on someone else's intellectual property and that we are protecting our own assets. As the team leader, I coordinate all of these processes and, in the case of ERB-041, for two different therapeutic areas.

> **Robert Michel**
> Companies need to adopt the process of generating teams, identifying team leaders, and developing a team charter and mission. This forces the organization to become much more focused on specific objectives.

**MICHEL.** Everything we do in product development is so intertwined that one person or group can't do something without it potentially affecting another part of the project. For example, if there are regulatory issues our team needs to address, those issues may have an impact on the launch date, which then has the potential to affect manufacturing and drug supply, which could then alter the commercial strategy in terms of having the sales team trained in time, having the selling materials prepared, and so on. Every time something happens there is the potential for a ripple effect.

**BASS.** One of the benefits of this new structure is having concentrated expertise in a particular therapeutic area. By looking at programs from an indication perspective, versus a compound perspective, teams are now comprised of experts on a particular indication, which increases the effectiveness of the team.

**MICHEL.** This model is still a work in progress. We are going to learn more benefits as we move forward, but a lot is going to depend on the team members to be aware of opportunities where we can use this new structure and format for improving our development process. The ultimate goal is to get new

drugs to the market that better serve the needs of patients.

**JACOBSON.** The Learn and Confirm method allows us to achieve efficiencies across therapeutic categories. Instead of having five different groups working on an Alzheimer's drug, for example, there is one group working on five different Alzheimer's compounds. This way the company can develop expertise around a particular disease area or particular therapeutic platform. It's a process of being more efficient, more targeted, and more effective in drug development. This way we can identify risks early so that when we move into later stages of development, the Confirm stage, which is where the major expense of clinical drug development is, we have increased our chances of success.

## Barriers Overcome

*Wyeth team members say communications go a long way toward overcoming many barriers.*

**FIELDS.** We've all had different experiences. Team members need to be open to ideas and suggestions from their fellow team members.

> **Dr. William Jacobson**
> One of the important things that we can do is to bring in the commercial organization as early as possible. We need to make sure everyone is supporting what has to be done to get us to the end point.

**JACOBSON.** There are always things that interfere with our progress. People move within the organization, people leave the company, and people come into the company. When there are new people on the team, there's always an upside because there's a new perspective, but there is a downside in that those people have to be brought up to speed. We have to be able to incorporate different perspectives without slowing things down. That's always a challenge. Another challenge is ensuring that as the team addresses a problem, it will ultimately come up with a concrete recommendation, not simply a list of options. Yet another challenge is that everyone on the team, with the exception of the team leader, has a "day job outside of the team." The team leader's job is to lead that team and to represent that team to senior management. The thing that sometimes gets in the way is the rest of the world.

> **Damon Bass**
> Senior management has empowered the people who report to them with the ability to make independent, sound decisions. As this happens, a cross-functional team operates with efficiency.

**MICHEL.** The biggest potential obstacle, and our team has been able to successfully avoid it, is that team members represent a line function. The challenge is to align the line management function's goals and objectives with those of the team's. That's where the skill of the team leader becomes important.

**FIELDS.** On a good cross-functional team, you don't hear "we can't do this." You hear, "here's another option that we can do and that would achieve the same objective." Everybody realizes very quickly that he or she can't achieve the company's objectives without everybody else on the team. Usually, given the information available at the time a decision is made, there is one best course. This course may be more difficult for one department or another. So when the team makes a decision, it might impact negatively on one department and positively on another. A good team will have members that will accept this and take the best course.

## Lesson Learned

*While the Learn and Confirm structure is still new within the company, Wyeth team members say the model likely to lead to efficiencies and help them better achieve their goal of getting better products to the market.*

**MICHEL.** One of the key benefits of having multidisciplinary teams is that an individual's skills can be strengthened. A team structure helps identify leaders in different areas. And as people grow within their roles within teams, as a by-product, the company is cultivating leaders for the organization. There are obvious benefits to be realized outside the immediate project.

**FIELDS.** Our basic objectives as a research organization can only be achieved through cross-functional teams. Everyone needs to understand what his or her role on the team is to facilitate the team's objectives. There has to be a corporate culture that understands that the process works best through a team approach. Wyeth has that team culture. For cross-functional teams to be effective, there needs to be senior management support of the culture.

> **Dr. F. Owen Fields**
> No one's role exists within a vacuum. On teams, everybody realizes very quickly that he or she can't achieve the company's objectives without everybody else on the team.

**BASS.** Senior management has empowered the people who report to them with the ability to make independent, sound decisions. As this happens a cross-functional team operates with efficiency.

**JACOBSON.** A best practice process is to listen to the people who know the product, the project, and the data. Sometimes organizations tend to forget that. Understanding strategic and tactical thinking and making sure the two are aligned is also part of what teams have to do. Effective drug development has to start with the end in mind. We do excellent science, but the end point is to develop drugs that can be registered and that address an unmet medical need. The goal is not simply to complete a trial. We can get so immersed in what it is we're doing — making sure the trial is on time or making sure the documents are filed appropriately, and so on — that we can forget what our goal is at the end of the day. From my perspective, one of the most important things that we can do is bring the commercial organization in as early as possible; this is absolutely essential. We need to incorporate commercial input early on, make sure it's front and center in our thinking, let it guide us, and make sure everyone is supporting what has to be done to get us to that point. ✦

To access a FREE Podcast on this topic, featuring Dr. William Jacobson, go to pharmavoice.com/podcasts.

serono
biotech & beyond

## Unmet needs.


We've developed many of the world's leading medicines for multiple sclerosis and fertility. We offer innovative drug delivery options for children with growth hormone deficiency. And we're working on more than 25 potential new therapies for cancer, autoimmune diseases, and other illnesses. We're one of the world's leading biotech companies. And our values and concerns are reflected not only in our products, but in our programs of patient education and support, such as MS LifeLines℠, Fertility LifeLines™, Connections for Growth® and SeroCare℠.

For a hundred years, the people of Serono have been focusing on significant unmet medical needs. Meeting them. And helping people live more fully. Embracing life. Enhancing life. That is the spirit of Serono.

seronousa.com

# NOVARTIS
## Integrated Discovery From the Start

The focus for Novartis Institutes for BioMedical Research (NIBR) is in the areas of discovery chemistry, developmental and molecular pathways, discovery technologies, epigenetics, genome and proteome sciences, human genetics, models of disease, and translational research. Research is conducted into oncology, neuroscience, autoimmunity and transplantation, respiratory, gastrointestinal, musculoskeletal ophthalmology, diabetes, infectious disease, and cardiovascular conditions.

When Novartis moved its global research headquarters to a former candy factory in Cambridge, Mass., in April 2004, it had an opportunity to revamp some of its processes for drug discovery. In fact, the transformation of the former Necco candy site into a state-of-the-art laboratory was designed to encourage collaboration, from open lab space in some areas the length of a football field to the glass walls of the offices and conference rooms, to the open halls and elevators.

Additionally, the company added new technology and new teams of scientists and researchers. One such team is the Developmental and Molecular Pathways group, which is applying a multidisciplinary approach to elucidate the best therapeutic intervention points within these networks.

The team's mission is to tackle drug discovery from a signaling pathway perspective versus focusing at the outset on specific targets and traditional disease areas. The short-term goal is to investigate disease-associated signaling pathways as collections of possible therapeutic targets by using sensitized cell-based assays that model a disease state to identify gene and compound modulators (drug targets and leads). The long-term goal of the Pathway Team is to develop a robust, somatic cell, genetics-based process to predictably, reliably, and systematically move from a pathway/disease link to validated targets and lead compounds.

Another new group is the Global Discovery Chemistry team, "Chem G," which focuses on the design and synthesis of potential drug molecules. Spanning various disciplines, this group works in teams to study these molecules and select those that have the greatest potential to help patients.

These two groups are working together, along with outside collaborators, to research cell-based assays to look for novel modulators of pathway. Thus far, the teams have identified several different independent chemical scaffolds, and the target for one of those has potential in oncology applications, particularly multiple solid tumors.

### Meet the **Novartis Team ...**

**Novartis Institutes for BioMedical Research (NIBR), Cambridge, Mass., is the global research organization of Novartis, a world leader in developing medicines to protect health, treat disease, and improve well-being. For more information, visit nibr.novartis.com.**

**DANIEL CURTIS, PH.D.**, is Investigator, Developmental and Molecular Pathways. He came to Novartis three years ago and has initiated successful external partnerships with biotechnology companies. He also serves on the Joint Research Committee for these relationships.

**PETER FINAN, PH.D.**, is Director, Pathway Biology, Developmental and Molecular Pathways. For the past eight years, Dr. Finan has led a number of target discovery, target validation, and drug-discovery projects, mainly in the field of PI 3-kinase research.

**MARK FISHMAN, M.D.**, is President of NIBR. He leads all worldwide discovery research activities of Novartis in Europe, the United States, and Japan.

**JOHN A. TALLARICO, PH.D.**, is Head of Chemogenetics, Global Discovery Chemistry Group. He came to Novartis in March 2004 and established the new research team focused on chemogenetics.

> **Dr. John Tallarico**
> The groups have to have a shared mission and shared goals before they even start the project.

## The Team Structure

*The establishment of the new research organization gave Novartis the opportunity to field multidisciplinary teams right from the start.*

**TALLARICO.** Chemical genetics work had been going on in the company for years. There might have been one guy banging away at a particular problem, asking for help from different disciplines, but it was very ad hoc.

Doctors' Choice Awards Luncheon
Thursday, October 19th, 2006
Grand Hyatt New York

# Want to increase your product's marketshare?

## Put one of these on your shelf


**80% of ads that have won the Doctors' Choice Award have seen an increase in marketshare**

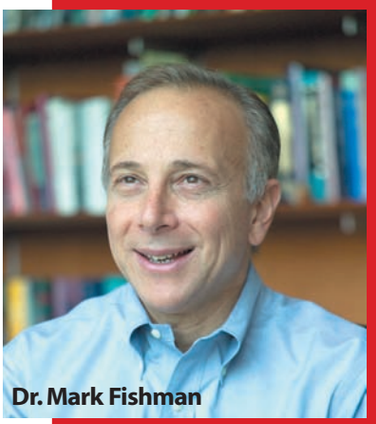
The Doctors' Choice Awards are unique in the number of ads evaluated, the size of the audience approached, and the response level obtained. In fact, the awards are seen as breaking new ground in audience feedback research on advertisements.

For more information go to
www.amponline.org
or contact us at amp-office@att.net

The DOCTORS' CHOICE AWARDS
Recognizing the Power of Medical Advertising

AMP
Association of Medical Publications

The mission of Novartis Institutes for BioMedical Research (NIBR) is to improve the drug-discovery process by pursuing a comprehensive, multidisciplinary approach that integrates novel concepts and tools across multiple disease areas.


Dr. Mark Fishman


Dr. John A. Tallarico


Dr. Peter Finan


Dr. Daniel Curtis

There was no formal process for cooperation. Now, we have processes that allow for a much more rapid, productive, and reliable way to achieve results than what was done before.

**CURTIS.** Novartis invested in cell-based screening, but now there is a team whose mission is to go beyond cell-based compound activity and to identify targets and use that information to help optimize the compound and resources.

> **Dr. Daniel Curtis**
> We believed from the beginning that to attack these particular problems we needed to build bridges early on in the therapeutic areas.

**FISHMAN.** By definition, all projects have a multidisciplinary component; the difference is how the teams are organized. Teams can be organized around a particular disease, but to my mind that is a narrow definition of a team. Teams should cross over different disease areas and between totally different disciplines. In my opinion, it's completely impossible to run discovery without multidisciplinary teams. One of the ways to break down barriers has been to have positions that cross over apparently unrelated areas. Another approach is to bring together a group that evaluates how different approaches can be brought to bear in relation to the patient. Teams can also be organized around a group of related targets and how to approach those targets.

**FISHMAN.** We have many new structures. Classically, the groups were quite partitioned from each other. With more mechanism-based projects, going all the way from research through development — and because mechanisms are shared among diseases — we found it imprudent to continue operations within silos.

## Why the Team Works Well

*A shared vision and a willingness to build bridges with other areas early on have helped the Novartis team achieve its goals.*

**FINAN.** One reason the team approach is successful is the physical location; the whole team is in the same building and we're close to each other. That doesn't mean that collaborations outside the company aren't handled well, but it's easier and faster to evaluate new thinking and new ideas being in the same location.

**TALLARICO.** Everyone in the "Chem G" group has a shared vision. And we know that the groups who work with Dr. Curtis and Dr. Finan share this vision as well. We are all pulling in the same direction.

**CURTIS.** We're not questioning every six months whether we have to rejustify the mission. This has allowed us to make a long-term investment in the external collaboration and in the technologies that we're bringing to bear.

**TALLARICO.** Because we're focused on basic science problems, it would be very hard for us to manage all of the other aspects of drug discovery, including pharmacology, animal, early clinical — all the activities that add to the complexities of drug discovery. When we've needed this expertise, there are colleagues in NIBR who are willing to help us. What is really important is that we communicate early and often about what is going on. Keeping people engaged in what's going on makes it easier to get these other activities done.

## Lessons Learned

*A new organizational structure, considerations about technology, and resource allocation provided the Novartis team with challenges, but also opportunities for growth.*

> **Dr. Mark Fishman**
> Multidisciplinary teams do speed up the whole process, and this model is cost-efficient because the mechanisms are shared between the different disease areas.

**FISHMAN.** The lesson I've learned is that everybody is different in terms of their talents and leadership. The challenge is capitalizing on each team member's strengths in the most efficient manner.

> **Dr. Peter Finan**
> What we are developing is a biotech feel within a big pharma organization. To achieve this, the team members have to have a certain personality in addition to the science background.

**TALLARICO.** We represent a completely new organization within Novartis. We have the same goal as the parent company, which is to discover drugs and add value to the drug-discovery pipeline, but we are doing things in a different way.

**CURTIS.** So much of our research should be focused on innovative processes, which is admittedly not easy. It's very difficult to identify how a compound's activity affects the cell and then try to define the efficacy target in the cell that mediates the activity. This is high-risk science, but it's also a high-reward activity. So the question becomes how to balance these approaches with more traditional means. This is a learning process of how to best use our energies most efficiently.

**TALLARICO.** Certainly, within this group, there is no fear about trying something new. That's really important. We don't have the endless hemming and hawing about the value of these experiments. We do our own critical analysis; if the answer is yes, this is a good idea, then we do it, pilot it, and show that it works, then apply it to our products. If the idea doesn't work because the experiment doesn't work or it is too complicated, that's just the way it is. We move on to the next good idea. But we should never be afraid to run the experiment.

**FINAN.** We're developing a biotech feel within a big pharma organization. To do this well, people need to have certain personalities in addition to having the science background. ✦

# KALYPSYS
## Focused on Evolving Processes

The transformation from a company that used technology to generate development drug candidates to a fully integrated biopharmaceutical company can be a long and bumpy road. No matter how many challenges, the teams at Kalypsys Inc. are not afraid to reinvent and challenge themselves. Kalypsys was founded in 2001 as a spin off from the Genomics Institute of the Novartis Research Foundation (GNF).

From the start, the company had a suite of ultra-high throughput screening, chemical, biological, and informatics technologies, which provided it with fully integrated drug-discovery capabilities. The company uses proprietary automated technologies to aggressively profile small-molecule drug leads very early in the discovery process and thereby enhance and accelerate subsequent drug-development activities through to clinical proof-of-concept.

One of the more promising projects is a new molecular entity that will be used topically to treat neuropathic pain. This program will go from concept to clinic quickly, taking about 21 months.

Kalypsys is preparing to submit an IND this year for the inducible nitric oxide synthase (iNOS) inhibitor, also known as KD7040. The initial neuropathic indication will be postherpetic neuralgia; other potential indications include diabetic neuropathy, lower back pain, and carpal tunnel syndrome.

### A Team Approach: From Concept to Clinic

*Members of the Kalypsys cross-functional team are transitioning along with the compound as the product moves from concept to clinic in just under two years.*

**MCKEARN.** To our knowledge, there hasn't been a company that has brought a topical pain program from concept to clinic, let alone to do so in 21 months. This is a huge challenge, one that we have embraced with enthusiasm. To our knowledge, the industry has recycled all topical pain medications from existing clinical or marketed compounds.

**HASSIG.** We were working on developing an oral agent, but it became clear as we progressed through chemical series that the properties were actually more suitable for a topical approach. We spent some time banging our heads against the wall going after the oral application, and then the team realized that the company was sitting on a gold mine. So we transitioned the program into a topical application for the treatment of peripheral neuropathies.

> **Dr. Chris Hassig**
> We're in a constant state of evolution. Our aim is to perfect the way we operate so programs that originally took a few years to get through proof-of-concept can now be done much more quickly.

**SCRANTON.** Chemists who originally synthesized the molecules are members of the development team. Pharmacologists and biologists transition with the project through discovery into development. These practices make transitions from discovery to development fast, efficient, and seamless. Everyone who has worked on the drug from the very beginning is on this team. We're learning that this is an extremely efficient model. When we embark on other compounds, we can take these learnings and apply them to other compounds or therapeutic areas.

**MCKEARN.** People who have experience with drug discovery are paired up with those who have development experience, and even with those who have never been part of the development process. This provides each team with

### Meet the Kalypsys Team...

**Kalypsys Inc., San Diego, is a biopharmaceutical company that uses proprietary automated technologies to profile small-molecule drug leads early in the discovery process and thereby enhance and accelerate subsequent drug development through clinical proof-of-concept. For more information, visit kalypsys.com.**

**CHRIS HASSIG, PH.D.**, is a Principal Scientist in the company's biology department. Additionally, Dr. Hassig is the project leader for the KD7040 Topical Gel program for neuropathic pain.

**JOHN MCKEARN, PH.D.**, is President and CEO. Dr. McKearn also is a member of the company's board of directors.

**SHAWN SCRANTON, PHARM.D.**, is Director of Clinical Development. He heads the clinical development for the three development phase programs.

Kalypsys has compiled a large chemical "drug lead" library and leverages an integrated drug discovery, medicinal chemistry, and experimental medicine team. Its mission is to discover, develop, and commercialize its products, alone and with strategic partnerships in multiple therapeutic areas.

Dr. John McKearn

Dr. Shawn Scranton

a healthy mix of experiences and an environment to train the next program leaders.

**SCRANTON.** There are no set rules for when companies should form a cross-functional project team. At Kalypsys, we've found success in forming these teams early. People get to know each other from program inception, and by the time the team is fully integrated, the team members are making really good decisions.

> **Dr. John McKearn**
> We're not afraid to reinvent and challenge ourselves as long as it leads to better integration, better results for our investors, our employees, and most importantly our patients.

**MCKEARN.** There are a hundred little decisions that happen every day. Without a team-oriented process that allows people to communicate and contribute their wisdom and passion, I don't believe a team can work at optimum efficiency.

**HASSIG.** In our development team meetings, it's clear that having experts in each of the disciplines enables us to come up with new directions, and we can catch issues before they become problems.

**MCKEARN.** It's great for teams to be focused, to be empowered, and to think outside the box. But teams shouldn't think so far outside of the box that they lose their focus. They need to consider the end goal, what might be missing, and what they can do to improve the quality of the compounds that are progressing into the clinic.

> **Dr. Shawn Scranton**
> It takes time for a team to form as a unit. Usually, it takes a hardship or two for a team to really begin to function well together.

## Team Barriers

*As the goal of the company is to find the most efficient and expeditious path to clinical proof-of-*

*concept, Kalypsys teams face their own sets of challenges.*

**MCKEARN.** In the first couple of years, Kalypsys could have been characterized as a company that had innovative technology. But the company has become an organization that sustainably reinvents and evolves the discovery and development process to provide the company with a robust clinical pipeline.

**SCRANTON.** Multidisciplinary teams have been empowered to guide key decision making and program-planning functions. They also have been given a forum by which they can receive guidance from senior management on an as-needed basis. This provides for rapid feedback, and thus maintains the momentum and efficiency.

**HASSIG.** This aforementioned forum also provides for cross-program learning. This has helped the entire organization keep apprised of the rapidly progressing program plan and to evaluate whether a learning from one project can be applied to another. Another point worth mentioning is that the forum provides an additional opportunity for employees who don't have a team affiliation to learn about development even if their focus was originally on discovery.

**MCKEARN.** We are willing to change just about anything to further or improve outcomes. As a small company, we can't compete with dollars or with the number of people on

## Sound Bites from the Field

**PHARMAVOICE ASKED THOUGHT LEADERS FROM COMPANIES SERVING THE PHARMACEUTICAL AND BIOTECHNOLOGY SECTORS: WHY DO YOU THINK CROSS-FUNCTIONAL TEAMS ARE IMPORTANT? WHAT OBSTACLES DO THIS TYPE OF MODEL POSE? AND WHAT ARE THE PROS AND CONS OF MULTIFUNCTIONAL TEAMS?**

**STEPHEN CUTLER** is Senior VP, Global Project Management, at Quintiles Transnational Corp., Research Triangle Park, N.C., a leader in pharmaceutical services, working to improve healthcare worldwide by providing innovative, quality, professional expertise, and market intelligence. For more information, visit quintiles.com.

"Given that one of the objectives of a project team should be to kill a drug as quickly and as cost-effectively as possible — if it is unlikely to be safe, effective, or commercially viable — representation from all the key disciplines is essential. Marketing, clinical pharmacology, toxicology, manufacturing, clinical pharmacovigilance, and so on, all need to provide key input to ensure the sequence of "hurdles" is jumped to bring a new compound to market. Too often in the past, large investments have been made in moving a drug toward the market only to find that, on arrival, the market has disappeared or had been seriously overestimated. The active involvement of key stakeholders at an early stage will help to ensure that the critical questions are asked (and answered) along the path to the market, thereby improving the quality and timeliness of decisions."

**GREGG DEARHAMMER** is President of i3 Statprobe, Ann Arbor, Mich., a provider of comprehensive, integrated data-services solutions for the pharmaceutical and biotechnology industries across all phases of research. For more information, visit i3statprobe.com.

"Obstacles preventing success of multidisciplinary teams include selective participation, inadequate representation, and lack of management support. Selective participation, or a de-prioritization of the team by its members, is rooted in the additional time investment required by team members and the lack of perceived benefit. Inadequate representation of all stakeholders, including contract research organizations, third-party vendors, and so on, prevents efficient and knowledgeable decision making. Team members will take their cue from senior management, who must demonstrate that their commitment to the process is clear, consistent, and participatory in nature."

**GLORIA GIBBONS** is Regional President, Europe, at Ogilvy Healthworld, London, a global healthcare communications organization. For more information, visit ogilvyhealthworld.com.

"A multidisciplinary team approach is the key to smarter working practices and pharma sector growth. Multidisciplinary teams are core to the way Ogilvy Healthworld works as an agency — whether it be to build stronger brands, re-engineer pharma business models for global and regional activity, or bridge the gap between R&D and commercial to bring products to market quicker and more effectively. The best solutions take into account all perspectives. The biggest and best ideas are channel-neutral at heart. There is no room for silo thinking in the pharma environment we all practice in today."

**JOHN KANE** is Principal and Managing Director, Kane and Finkel Healthcare Communications, San Francisco, a full-service healthcare communications agency. For more information, visit kaneandfinkel.com.

"Multidisciplinary or cross-functional teams can have a major impact in providing a company with a competitive advantage. How many times as a marketer have you been given clinical data that's the foundation of a promotional campaign and thought, 'If only marketing had been involved sooner?' Now, more than ever, we are seeing the clinical-development teams collaborate with marketing teams to develop clinical trials that are scientifically rigorous and, at the same time, provide data that are differentiating and can be leveraged in promotion. By including marketing in the clinical-trial process, the clinical-development teams can tap into the understanding of market needs and physician mindset that can be the difference in the battle for market share."

**SUSAN MILLER** is Partner of The CementWorks LLC, New York, an independent healthcare agency. For more information, visit thecementworks.com.

"Why are multidisciplinary teams important? In a word: efficiency. Teams that work in silos create unnecessary redundancies and often fail to take advantage of internal resources or learnings that exist in other areas of an organization. Multidisciplinary teams bring all the necessary stakeholders to the table in a timely fashion so that good ideas are expedited and bad ideas are killed

a project. One of the ways that we can compete is with more information at each critical decision point. If we have more quality information earlier, then we're making better decisions for compounds as they move forward in the clinic.

## Lessons Learned

*Members of the Kalypsys development team discuss best practices for building successful cross-functional teams.*

**HASSIG.** We ask a lot from each team member, as if they are playing offense and defense for the entire time. While we get a good workout, at the end of the game we have a more cohesive unit that can make better informed decisions.

**SCRANTON.** When everyone is a member of the team, then the team starts to function as a unit. It is this unit that provides a program with efficient and sustainable progress.

**MCKEARN.** We try to operate by the principles of chemical urgency — know the liabilities of a compound or chemical series in the early days of its life. We're trying to do R&D the right way. We're trying to do it differently. We're not afraid to reinvent and challenge ourselves as long as it leads to better integration and better results for investors, our employees, and most importantly, the patient. ✦

PharmaVOICE welcomes comments about this article. E-mail us at feedback@pharmavoice.com.

posthaste. Theoretically, multidisciplinary teams build on a broader range of experience and can tap into deeper corporate resources. They can also manage up and down the various chains of internal command to help facilitate change or institute new approaches. It is easy for one voice to be drowned out in a large organization, but a project that has multiple champions may stand a better chance of coming to fruition."

**MYCHELLE MOWRY** is VP for Global Health Industries, Oracle Corp., Redwood Shores, Calif., an enterprise software company. For more information, visit oracle.com.

"An extension of the R&D and marketing partnership is the involvement of other cross-functional teams to enhance both the efficiency and effectiveness of the development and launch process. Cross-functional teamwork compresses development cycle times and increases a product's speed to market through close coordination of efforts and earlier resolution of downstream problems related to regulatory approval, manufacturing capacity, and salesforce support. It is also valuable in developing a well-rounded product launch strategy by leveraging the knowledge and capabilities of diverse teams."

**JOHN RACIK** is President and CEO of Stonefly Communications Group, Westerville, Ohio, a customer-centric healthcare advertising agency and an inVentiv Health company. For more information, visit stoneflygroup.com.

"Integration allows pharmaceutical teams to plan more strategically by beginning the process with the end in mind. A multidisciplinary team can plan around not only the scientific or medical goals of the product, but more importantly, the value that the product can ultimately bring to the customer. Establishing a common understanding of where the team wants to take the product helps ensure all disciplines will be working collaboratively to achieve immediate and long-term brand success. With the diversification of the brand's customer base (including HCP, patient, MCO, government, etc.) over the years, the move toward multifunctional teams not only improves efficiency when developing new drugs, but also drives what we term "market efficacy." Market efficacy is the strength to answer the functional, practical, emotional, and value needs of the brand's entire customer base. Establishing drug-development protocols with a purely scientific focus can lead to an effective, but undifferentiated brand. In other words, it remains a product and not a brand. People rarely buy products, they buy brands. In a multidisciplinary team, marketing becomes part of the conversation earlier. Discussions around how the product will be differentiated and what unmet needs it will fulfill for customers happen in the earliest stages, when there's still an opportunity to impact the design of the clinical trials and prescribing information."

**HANNEKE SCHREURS** is Senior VP, Global Project Management, Omnicare Clinical Research, King of Prussia, Pa., a Phase I to IV contract research organization that provides drug-development services to pharmaceutical, biotechnology, and medical-device companies in 30 countries. For more information, visit omnicarecr.com.

"The success of a clinical trial is never linked solely to one facet of the drug-development process. Rather, a variety of functional areas must work together to achieve a common goal. As such, the most effective organizations structure themselves using multidisciplinary teams. This client-centric approach places project management at the center of the business with the supporting services reporting into the teams who manage and conduct the trials. This strategy helps to ensure consistent communication, proactive solutions, and accountability at every step of the process."

**PETER SOWOOD, M.D., PH.D.**, is President of Icon Clinical Research, Europe, London, a global provider of outsourced development services to the pharmaceutical, biotechnology, and medical-device industries For more information, visit iconclinical.com.

"The use of multidisciplinary teams to manage clinical trials is good practice because this ensures better communication flow across key disciplines, keeping the team focused on the core objectives, critical milestones, and overall project success. Involving all disciplines in the planning and implementation of the project takes advantage of the individual functional knowledge, expertise, and experience and contributes to a more cooperative, cohesive, and successful project team. The combined domain knowledge of multidisciplinary teams improves awareness of issues and consequently enables better risk-management and contingency planning. Team cooperation also maximizes the use of resources and avoids duplication of workload, while providing a forum for the development of successful strategies."

**STEVE VIVIANO** is President of Integrated Communications Corp., Parsippany, N.J., a full-service healthcare advertising agency. For more information, visit icclink.com.

"The use of multidisciplinary teams in pharmaceutical product commercialization is here to stay. The complexity of issues faced on a day-to-day basis requires the perspective and expertise from a broad range of disciplines to maximize opportunities. It is important for the team to share a common vision and have a leader who understands what each constituent brings to the table. It is also imperative for the individuals on the team to respect one another's priorities and to be sensitive to the fact that many will be members of several other teams, each with its own challenges and demands. When the chemistry is right, the results far surpass what could be achieved separately, and the process works quicker and more efficiently."