

Cover Story

With one eye on the rearview mirror and one eye on the road ahead, pharma and biotech experts predict what lies ahead for drug discovery and development.



Just as one season transitions to another, drug discovery and development processes face change—scientific changes, regulatory changes, and business changes. As Drug Discovery & Development magazine marks its 10th anniversary of publication, we invited pharmaceutical and biotechnology companies and industry suppliers to reflect on the history and forecast the future. We also surveyed magazine readers to measure the successes of the last 10 years and the potential of research for the next decade. We share some of those comments here. But there's much more, including more commentary, company profiles, and intriguing "bold predictions" here on www.ddmag.com

Cancer research is key

Researchers surveyed expect the greatest advances in the next decade to come in cancer therapies; but, it is there that they also see the greatest challenges. Established in 1998, [Gemin X Pharmaceuticals](#) is developing cancer therapeutics based on activating the natural process of apoptosis and inducing growth-inhibiting metabolic changes in cancerous cells. The company currently has three clinical development programs underway.

"Prioritization of clinical pathways, oncology market opportunities, and potential strategic collaborations will be important over the coming years," says Glenn Gormley, MD, PhD, president and chief executive officer. "More broadly, we need to address the growing inefficiency of drug discovery, development, and commercialization."

Infinity Pharmaceuticals, Inc. is an even newer player in cancer therapies.

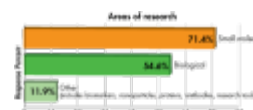
"Our pipeline at Infinity did not exist 10 years ago; not even five years ago," reports Steven H. Holtzman, chair, president and chief executive officer. The company focuses on researching emerging cancer targets, such as heat shock protein 90 (Hsp90) and the Hedgehog signaling

pathway. A Phase 3 registration trial evaluating Hsp90 agent IPI-504 in refractory gastrointestinal stromal tumors (GIST) is scheduled to commence in 2008. Infinity is also advancing an oral anti-chaperone agent, IPI-493, currently in Phase 1 development. A third candidate, IPI-926, targets the Hedgehog signaling pathway and is poised to enter Phase 1 evaluation by the end of 2008.

A shifting lineup

Of those surveyed, (Figure 1) more than half (55%) said they were involved in research for biological therapies, but small molecule drugs still hold a firm lead. More prevalent, however, are acquisitions and collaborations between academia, research organizations, and companies large and small.

Alkermes, Inc. is a biotech company with a pipeline that includes extended-release injectable, pulmonary, and oral products for the treatment of chronic diseases, such as central nervous system disorders, addiction, and diabetes. Currently, three compounds are near the commercial stage, according to Richard F. Pops, the company's chairman. "In 10 years, it will become clear that the majority of truly innovative drugs in development will have originated within biotech companies," he says.



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Figure 1: Current areas of research (multiple responses allowed).
Source: Drug Discovery & Development reader survey, 2008.

In just six years, **PolyMedix** has moved two biomimetics drugs—a novel antibiotic drug and a unique heparin antagonist—to Phase 1 trials with a handful of employees and expending less than \$17 million per drug. How did they do it? "We have succeeded more quickly and on far less money than big pharma efforts in these areas because of our proprietary

computational drug design technology, originally developed at and exclusively licensed from the University of Pennsylvania," says Nicholas Landekic, president and CEO. But, access to capital for further development will be a challenge, he reports.

In 10 years, Landekic adds, "Ideally, we will be selling our own acute care drugs for infectious diseases and cardiovascular disorders in the North American hospital market. However, it is probably more likely that, given the dry pipelines across the big pharma companies, PolyMedix will be acquired and its products absorbed into a larger organization."

A successful small pharma/biotech company can be an attractive target for big pharma. In June, 2008, **GlaxoSmithKline** (GSK) acquired **Sirtris**, a four-year-old company focused on aging and metabolic diseases. The resources of big pharma will help expedite the development process, says Christoph Westphal, MD, PhD, chief executive officer of Sirtris. "We'll see the industry continue to move toward an improved acquisition model—exemplified by GSK/Sirtris—where research-driven biotech companies will operate autonomously and maintain their entrepreneurial culture, while leveraging the development/commercial expertise of big pharma."

Positive Impact: Biomarkers

Merck & Co., Inc. reports that it has worked with the US Food and Drug Administration (FDA) and the Critical Path Initiative to establish a flexible, practicable process for identifying and validating new safety biomarkers that would be most useful within a regulatory environment—those that could potentially be used in both the pre-clinical and clinical settings.

By far, biomarkers will have the greatest positive impact in the next decade, readers said. During the past decade, researchers collectively ranked biomarkers as the eleventh most positive factor. For the next decade, it is number one.

How have the following contributed to advances in drug research?

	Positive Impact	
	Last 10 years	Next 10 years
Biomarkers	78.4%	97.2%
Access to Research Information on the Internet	88.2%	92.7%
Genomics	91.0%	91.3%
Proteomics	81.7%	90.9%
Bioinformatics	79.5%	90.1%
Imaging	87.4%	89.6%
Molecular Biology	92.9%	87.5%
Genetic Animal Models	88.0%	86.7%
<i>in vivo</i> Analysis	82.4%	85.3%
Diagnostics	78.7%	84.9%
Access to Early-stage Research	74.7%	82.1%
<i>in vitro</i> Analysis	82.9%	81.6%
Nanotechnology	81.2%	80.0%
RNAi	60.7%	75.3%
Availability/Management of Data	69.4%	73.5%
HCS/Microscopy	65.1%	73.2%
High Throughput Screening	77.1%	73.1%
Personalized Medicine	41.5%	72.0%
<i>in silico</i> Analysis	55.8%	71.1%
Safety Assessments	64.8%	68.3%
Availability of Skilled Personnel	60.1%	63.0%
Globalization	54.7%	57.7%
Funding	44.7%	51.6%
Outsourcing	46.2%	46.8%
Research Conducted Offshore	37.0%	44.7%
Availability of Trial Participants	32.7%	44.3%
Regulatory Oversight	28.5%	36.3%

Mergers and Acquisitions	20.6%	21.6%
Bureaucracy Issues	6.6%	11.5%

The biggest challenge for research and development in the cardiac safety arena is to find a method of determining risk for each individual because the clinical trial settings cannot be used to rule out rare occurrences," says Sasha Latypova, co-founder and executive vice president of **iCardiac Technologies, Inc.**, a developer of ECG biomarkers. The company believes that ECG-based cardiac safety analysis will migrate to the diagnostic and clinical settings and even to home monitoring of at-risk patients.

"Biomarkers will accompany the development of virtually every new drug. They will be used to assess efficacy and safety/toxicity," predicts Dennis Harris, chief scientific officer, **Millipore Corporation**. "Companion diagnostic assays (biomarkers) will follow the drug through the clinic and into patient care."

Positive Impact: Personalized Medicine

Personalized medicine will be a major force in how companies develop drugs, according to nearly three-quarters of those surveyed, a big jump from the previous decade, where only 42% said it played a positive role.

"In 10 years I predict that AVEO will have successfully brought our novel cancer therapeutics to market by matching our molecularly targeted drugs to responsive patient populations, and will remain at the forefront of realizing the vision for personalized medicine in cancer," says Tuan Ha-Ngoc, president and chief executive officer, of **AVEO Pharmaceuticals**.

"The industry will have moved largely towards personalized medicine, where patients will undergo highly sophisticated testing to determine the best treatment options for their disease," says Brad Thompson, PhD, president and CEO, **Oncolytics Biotech Inc.** The biopharmaceutical company is conducting 12 clinical trials examining the reovirus REOLYSIN as a human cancer therapeutic.

Industry vendors see the personalized medicine movement changing the research tools they will offer. According to Nate Cosper, director of marketing, **Caliper Life Sciences**, "Drug discovery and development will occur in a bespoke fashion, [with] therapeutic regimens tailored for the specific biological profiles of individual patients. Combination therapeutics will be developed based on the protein expression profiles of patients, enabling safer, more effective treatment of disease. Genome sequencing will provide clinicians with exquisite data about a specific patient, ensuring a better overall disease management strategy."

Feedback from patients will be critical. "Consumers will be able to provide data/information to fuel innovation by exhibiting certain disease states or diseases that are part of their personal profile," reports Michael Naimoli, industry solutions director for **Microsoft's** US Healthcare & Life Sciences Group.

"A big challenge will be the continued adoption of microarrays as tools for routine testing in disease diagnosis and the FDA's acceptance of such approaches, says Jay Kaufman, vice president, Product Marketing, **Affymetrix Inc.** "This has implications for the kind of products we want to develop and offer. There will be ongoing interest in microfluidics and other miniaturizing technologies to try to drive costs down."

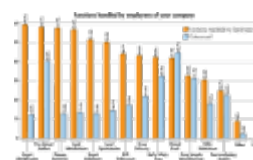
Trials on trial

Clinical trials are the most frequently outsourced task in the drug research process (45% outsourced versus 42% managed in-house, Figure 2), and the availability of trial participants is a growing concern.

BioMS Medical Corp. focuses on the clinical development of dirucotide, for the treatment of multiple sclerosis (MS). Shifts in the regulatory environment (some positive, some negative) and the emergence of new geographical areas for conducting trials, such as Central and Eastern Europe, have been factors. The major challenge will be enrollment of MS patients, due to increased research in the disease, says Kevin Giese, CEO and president.

Changing tools

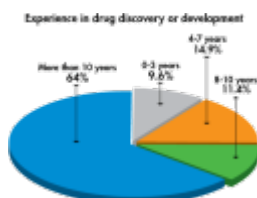
Back in 1998, high throughput screening (HTS) was a technology of great promise. While HTS did have a positive impact over the last 10 years (according to 77.1% of respondents), the anticipated impact for the next decade drops slightly.



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Figure 2: Research functions performed in-house versus outsourced. Source: *Drug Discovery & Development* reader survey, 2008.

However, bioinformatics and the availability/management of data are expected to play greater roles in the future (see Table), indicating a growing need for interpretation of results.

The availability of new tools and technologies and molecular biology studies will develop a better understanding of the biological mechanisms of various diseases. Imaging and in vivo studies remain a key component of drug research. According to **Nikon Instruments, Inc.**, advances in digital imaging have revolutionized how research is conducted, increasing data collection capabilities and ushering in an era where quantifiable data, previously measured by the researcher's eye, is empirically checked through a series of equipment, from microscope, to digital camera, to analytical software.



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Survey Respondents: Years of Experience

"One of the challenges will be learning how to translate multimodal in vivo imaging from small animals to larger animals and humans," says William McLaughlin, director of Research & Advanced Applications, **Carestream Molecular Imaging**. "In the future, we need to find higher throughput in vivo testing methods that help expedite drug discovery and development and optimize costs for drug developers and, ultimately, consumers."

Data integration and management are some of the greatest challenges that researchers face. "We have the capability to collect terabytes of data from multiple - omic sources ... from laboratory and clinical samples. Increasingly, the use of "biological fingerprints" or patterns of expression, posttranslational modifications, pathways etc., in the presence of modulators (small molecules and biotherapeutics) will drive drug discovery and development," says Dr. W. Blaine Knight, vice president of Drug Discovery at **Southern Research Institute**.

"Functional testing, in primary cells and other relatively complex systems, will replace pharmacologic screening based on potency at a single molecular target," says Patrick Dentinger, president and CEO, **Absorption Systems LP**, a preclinical contract research organization focusing on the ADME properties of drugs. "The outcome will be more effective drugs, but the challenge will be to develop structure-activity relationships around assays in which multiple targets may be involved."

François Degorce, head of marketing, **Cisbio Bioassays**, envisions three technology trends: more relevant assays, faster label-free technologies to speed up the high throughput screening process, and the need to study several parameters at the same time in a high throughput mode. "In the future, we will see more qualified assays using natural models," he says. "These formats will need to satisfy both sensitivity and cell handling. The introduction of cells into screening processes implies that cell production and quality can be closely monitored."

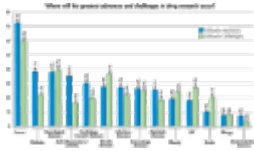


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Survey Respondents: Job Functions

"Biochemical assays will fade away," says Jeff Jensen, CEO, **Fluxion Biosciences**. "All screening and pre-clinical development will be done using cells derived from human stem cells. Clinical trial patient segmentation will require that early screening tools are adopted for patient stratification, and these tools ultimately become diagnostics in the clinic. Drugs requiring a companion diagnostic become the norm."

"Ten years from now, stem cell therapies will be mainstream and gene therapy back in vogue," says Jeff Mooney, **Corning Life Sciences**. "Microfluidics and nanotechnologies will make their way from the bench o the bedside (and home) allowing real time diagnostic monitoring and treatment."

"In the next 10 years we should expect to see innovations in methodology and/or hardware designs that will facilitate efficient screening of integral membrane proteins, which represent a challenging yet interesting class of drug targets," says Ger Brophy, general manager, Advanced Systems, **GE Healthcare Life Sciences**. "In addition, I predict a significant increase in the use of phenotypically-rich, cell-based models, based on differentiated cell technology, for advanced toxicology studies."



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 Figure 3: Advances/challenges for drug research. Source: *Drug Discovery & Development* reader survey, 2008.

"Drug research technology will not only need to release the researcher from mundane activities but will increasingly move from being the focal point," says David Harding, **RTS Life Science**. "The scientist's focus will increasingly return to the scientific problem at hand and away from the technology."

"The ability to create integrated workflows is key," reports Marijn E. Dekkers, president and chief executive officer, **Thermo Fisher Scientific**. "Scientists have increasingly less time to spend on this, and they're looking to technology companies to play that role so they don't have to spend their time developing the experiment—but rather are more focused on drawing conclusions from the results."

New operators?

While new technologies are creating excitement, other factors in the market—including mergers, acquisitions, outsourcing, and globalization—will create changes—or even seismic shifts.

"Large pharma will spend 20 to 40 percent of what they're currently spending on research with a large chunk devoted to contract research areas (CROs)," reports Richard Boehner, president, **Symyx Research**. "As it stands today, the standard CRO offering is not differentiated—it's very much a commodity offering—and over the next 10 years, that will change."

SRI International, a contract research organization envisions that government/academia will organize into three divisions: research, discovery, and development. Research will concentrate on transformational work. Discovery will advance hits/leads to product candidates. Development will translate biomedical opportunities to human efficacy. Pharma/biotech will refocus internally away from basic/applied R&D toward business development, commercialization, and sales/marketing; they will embrace open innovation, with most of their R&D outsourced.

"Company fortunes will no longer be made developing a few blockbuster drugs designed for the masses, but by developing masses of focused therapeutics, targeted specifically to a few," according to Robert J. Rosenthal, PhD, president and CEO of **ESA, Magellan Biosciences**.

"Maintaining scientific teams long enough to produce meaningful work could be a challenge because new drugs and technologies can require several years of effort by highly skilled scientists and engineers before success is realized," says J. Fred Pritchard, PhD, vice president, Drug Development, **MDS Pharma Services**. "Development and regulatory services companies that can maintain a stable R&D workforce will have the best chance to succeed."

"We are nearing the end of the era of the fully integrated pharmaceutical company, and are entering the era of the virtual drug discovery company," says Kevin Lustig, PhD, CEO and president, **Assay Depot**, which hosts an outsourcing marketplace for pharmaceutical research services. "The most successful drug discovery organizations of the future will be those that maintain core expertise in a few select areas while outsourcing most of their research activities."