

A Quest for DISCOVERY

The joy of uncovering a scientific breakthrough is a compelling driver for **Dr. Bob Sliskovic**. Having made his mark with a leading role in developing **Lipitor**, he is focusing his skills on new discoveries for small biotech and pharma companies as a research consultant for IDSC.



Optimism and resilience are the marks of a good pharmaceutical scientist. And Bob Sliskovic, Ph.D., has an abundance of both.

"In this industry, we need to get used to failure because we fail more times than we succeed," he says. "But what has always kept me, and hundreds of others like me, going is the hope that success is just around the corner. It's important to be persistent, to never give up hope, while at the same time 'know when to hold 'em and when to fold 'em.'"

That hope certainly has paid off in Dr. Sliskovic's career as he has enjoyed the rare good fortune of playing a leading role in bringing a product to market, and an exceedingly successful one at that: Lipitor.

That elusive holy grail of discovering something new that could help improve the human condition and bringing it to market

keeps scientists like Dr. Sliskovic in search of the next great compound.

"The anticipation of success is an extremely powerful stimulant," he says. "I've watched scientists receive the cruelest blows in terms of having a pet compound die, but the next morning they would be back and raring to go."

That resilience, persistence, and ability to bounce back from failures both amazes Dr. Sliskovic and continues to drive him forward.

"The majority of people who I've worked with over the years are driven forward by the hope that success is just around the corner," he says. "And as Scarlett O'Hara said at the end of *Gone with the Wind*, 'tomorrow is another day.' That's what we're always waiting for: tomorrow, the start of another day."

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It's certainly an attitude that has sustained him, particularly as Pfizer chose to close its Ann Arbor facility, where he spent 23 years of his working life. Rather than be bowed by the decision, Dr. Sliskovic, along with other Pfizer Ann Arbor veterans, found new and positive ways to move forward. (For more information on the emergence of new companies in the region, see box on opposite page.)

Today, as a director at International Discovery Sourcing Consultants (IDSC), Dr. Sliskovic brings that persistence and determination to projects in an effort to help its biotech and pharma clients achieve their own discovery and development successes.

IDSC provides advice and counseling on the whole drug discovery process, from early discovery to entry into human testing.

Experienced medicinal chemists, such as Dr. Sliskovic, can take on the role of running the research program for smaller biotech companies that don't have their own in-house

chemistry resources. (For more on IDSC's expertise and projects, see box on page 76.)

BUILDING Blocks

The natural world — the way things taste, look, feel, and smell — has always been a source of fascination to Bob Sliskovic.

"From a young age, I was always inquisitive about what made things taste the way they did, why there were different colors, what smells were made of, and so on," the scientist says. "As I entered high school and was introduced to chemistry these questions were still fresh in my mind, and I discovered that organic chemistry could provide me with some of the answers to these childhood questions."

The torch had been lit and the young student immersed himself even further in organic chemistry and its link to the natural world. As an undergraduate in chemistry, his focus had been on developing new molecules or new methodologies to help the field of synthetic organic chemistry, and it wasn't until he went on to his Ph.D. that he began to recognize that his love of research could be put into practical use through drug discovery.

Post-doctoral work brought him from the United Kingdom to the labs of Lederle Laboratories, then a division of the American Cyanamid Co. and now part of Wyeth, in Ann Arbor, Mich., and from there to an interview with the Parke-Davis pharmaceutical research division of Warner-Lambert in Ann Arbor.

For Dr. Sliskovic both the job and the location were a perfect fit. He stayed with the company, which later became Pfizer, until the facility closed in 2007, and, having grown to love his environs, chose to remain in Ann Arbor and join IDSC thereafter.

"What struck me about the facility was that it had a real family-type atmosphere; everybody knew everybody else," he says. "From early on I was surrounded by quality scientists doing quality science, all sharing the common goal of discovering medicines and having some fun along the way."

Among those quality scientists were two — Bruce Roth, Ph.D., and Roger Newton, Ph.D. — who were leading the work on the HMG CoA reductase inhibitor program.

"It was Bruce's seminal work that led to the discovery of this particular class of compounds from which Lipitor eventually emerged, and that was where I was involved," Dr. Sliskovic says. "Bruce had the initial discovery of the core structure of Lipitor. For one reason or another that class of compounds, which was really the basis of everything that followed, could not be advanced into development and I was called upon to do some fine-tuning on the

compound. These efforts finally became Lipitor. I was very fortunate to be placed in the right project at the right time and given the opportunity to fine tune this compound. I'm fortunate that instead of falling at the 99 meter mark of the 100 meter race, I, with lots of other people, crossed the tape."

MANAGING THE Ups and Downs

An essential element to being a good or great scientist is having a real love for the discipline. For Dr. Sliskovic, that passion for science was instilled in him by his graduate school professor and the flame was fanned throughout his career at Parke-Davis/Pfizer by his boss, Dr. Roth.

"I worked with Bruce side by side for virtually my entire career at Warner-Lambert; 23 years is a long time with the same supervisor,

and I owe a lot, if not most, of my success to his mentorship," Dr. Sliskovic says. "He is the best synthetic chemist I ever encountered."

Aside from encouraging real due diligence in scientific discovery, Dr. Sliskovic says he learned from Dr. Roth the importance of an enjoyable work environment.

"He has a great sense of humor and he brought a degree of lightness to the lab; when things were going bad, we just

kept going, knowing tomorrow would be a better day," Dr. Sliskovic says.

In his own leadership, both at Pfizer and today at IDSC, Dr. Sliskovic believes first and foremost in encouraging others by allowing them to take charge of projects.

"I've always encouraged other people to accept and to take responsibility for their

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REBUILDING A COMMUNITY

In 2007 Pfizer announced it planned to close its human health research and development facilities in Ann Arbor and Kalamazoo, Mich., leading to the loss of around 2,400 jobs in the region.

In Ann Arbor, the decision was a bitter blow for scientists such as Bob Sliskovic, Ph.D., now a director at IDSC, as well as for the city and for the South East Michigan region as a whole.

Ann Arbor and its links to the University of Michigan, both from a scientific and cultural standpoint, had captured the imagination of Dr. Sliskovic and many individuals like him.

"In terms of providing jobs for scientists, both full-time and on a contractor basis, then all the different functions — restaurants, stores, houses — that supported that facility, it was a real blow to the economy of this city."

With the help of organizations such as Mich Bio, a statewide consortium of companies in the life-sciences area, and Ann Arbor SPARK, an organization focused on the economic development of innovation-based businesses in the Ann Arbor region, there remains a determination to build the region as a biotech cluster. That goal is being driven forward by companies such as IDSC and Velcura Therapeutics.

"A whole host of smaller biotech companies are springing up to replace the void left by Pfizer," Dr. Sliskovic says. "Many of them are trying to team up with academia in this area; we have a number of world-class academic institutions. I think there are some really good fledgling steps that have been taken by companies such as IDSC to rebuild the life-sciences research in this area."

These companies have taken a page out of Kalamazoo's book, which has been rebuilding its scientific center after an earlier Pfizer site closure.

"Companies in the Kalamazoo area and Western Michigan University partnered to form an alliance that has reinvigorated that whole area, so hopefully this is a model we can replicate in South East Michigan," Dr. Sliskovic says.

Above all, it is the commitment of individuals like Dr. Sliskovic and others that makes this goal achievable.

"We are very fortunate that Bob and colleagues like him had an interest in coming to IDSC," says Mark Creswell, president and CEO. "Bob is a fine example of the many folks who chose to stay in the area because it's a wonderful community to live in. By going to work with local biotech companies, forming start-up companies, and partnering with other scientists in the area, they're able to really make a substantial impact on the drug discovery industry in this region."

actions,” he says. “Even when it’s a bit of a stretch for an individual I’ve found that 99.9% of the time people don’t disappoint,” he says. “If someone is given an opportunity to excel, they tend to excel.”

To that end, Dr. Sliskovic encourages people to follow their ideas and to take responsibility for their activities, giving them a sense of empowerment.

That approach fits well with his current position at IDSC and working in collaboration with external partners and clients.

“In big pharma, the tendency is to work internally with people you know, but when dealing with other companies it’s important to be more trusting of their abilities than you may be comfortable with, and that goes for them too,” he says. “The fact that I tend to give the benefit of doubt helps. And I don’t



These services range from technology to clinical development through CROs and even to discovery and development, creating an industry of “virtual” pharma and biotech organizations, in other words, a company that retains the intellectual property and a small core of specialists while outsourcing much of the workload.

International Discovery Sourcing Consultants (IDSC), which started up a year ago, has stepped into the mix to offer discovery chemistry and outsourcing services, from early discovery to entry into human testing, to pharma and biotech companies.

In addition, IDSC can become the virtual lab for smaller companies that may not have their own in-house chemistry resources.

want to build walls and create silos between companies, so developing a degree of mutual trust is essential in these relationships.”

The move from a large pharma company to a small drug discovery consultancy has been a positive one for Dr. Sliskovic and has allowed him to return to his real love of scientific research.

“When I left Pfizer I was managing 70 people, and as I moved up the managerial chain I tended to get further and further away from the day-to-day science and I really missed it,” he says. “Being in a smaller organization requires being more intimately involved with the science and these days I find myself conducting research and thinking of problems in a way that would have been unheard of in a big pharma company. For example, I have found myself thinking about designing synthetic routes in chemistry or possibly writing grant proposals.”

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It is, he says, a return to his roots and he believes the best use of his talents. Too often, he says, companies pull the best scientists out of the lab to be managers.

“I often envied the scientists I was managing because they were still involved in science,” he says. “Now I’ve come full circle; I started my career as a synthetic organic chemist and to some degree I find myself returning to synthetic organic chemistry.”

Dr. Sliskovic also appreciates the free flow of information between individuals and departments that is characteristic of smaller companies, noting that barriers between discovery and development started to become more pronounced during his career in large pharma.

“A wall has gone up between discovery and development; once a drug is discovered it’s thrown over the wall into development and

A VIRTUAL WORLD

THE GROWTH OF EMERGING BIOTECH AND BIOPHARMA COMPANIES HAS BROUGHT WITH IT A GROWING NEED FOR SERVICES THAT THESE SMALL ORGANIZATIONS OFTEN DON’T HAVE IN HOUSE.

“We can act as virtual VPs of research for companies, running their whole research program and designing a medicinal chemistry program for them,” says Bob Sliskovic, Ph.D., a director at IDSC.

Among the roles IDSC takes on is vetting CROs to make the compound for the client and then returning it to the client for evaluation.

“Then it’s an iterative cycle where we would again advise and help them with the design of additional compounds going forward,” he says. “So we can act as VPs of drug discovery and act as counselors for development for clients who are going into advanced clinical testing or early clinical testing. We can act as their virtual chemical development heads. And we can act as chief scientific officers giving opinions on targets.”

Aside from providing expertise on the whole drug discovery process, IDSC has a stable of therapeutic experts, from cardiovascular — Dr. Sliskovic’s area of expertise — to anti-bacterial, CNS, and so on.

Velcura Therapeutics, a small biotech company based in Ann Arbor, Mich., has engaged IDSC for help on the design and sourcing of medicinal chemistry data for its second generation and new bone therapy molecules.

Velcura recently received IND approval for one of its compounds, VEL-0230, and is now seeking to proceed into human testing. VEL-0230 stimulates bone formation and inhibits bone loss.

“Bob is providing both strategic oversight and chemical design expertise in our program to develop more potent bone disease therapies,” says Michael Long, Ph.D., CEO of Velcura. “His deep experience in the pharmaceutical industry has helped us rapidly advance our search for additional therapies.”

Having helped to design the compound, Dr. Sliskovic began the search for a CRO partner to make the compounds.

“We were able to find a CRO in the local area, so now we have three companies within about 15 miles of each other all working together — Velcura, IDSC, and AAPhar-masyn — which is a great model for other companies in the area to take on,” Dr. Sliskovic says.

With the growth of small biotech companies, Dr. Sliskovic sees a greater trend toward outsourcing and forming partnerships with other companies to bring a project to fruition.

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that's the last we hear of it," he says. "Twenty years ago it was a more intimate and intertwined relationship."

And while big pharma has been making concerted efforts to break down silos to allow a freer flow of information in discovery, barriers between discovery and development persist.

PERSEVERANT Focus

Having seen projects proceed through early discovery to IND filing to clinical trials to submission and commercialization, Dr. Sliskovic understands the rocky road of drug discovery and has sought ways to steer through them.

It's the next step — commercialization — that remains the end goal.

"I often look at this as a thousand-rung ladder and when we're in early discovery we're on the 20th or 30th rung of the ladder, so I have to remind the scientists I work with that there's another 900 rungs to go before we get to the market," Dr. Sliskovic notes. "There's lots of things that can go wrong."

Moving up that ladder requires perseverance, a clear, methodical approach to the task ahead, and an ability to know when to let go.

"I like to have everything tidy, with a beginning, a middle, and an end," he says. "In research, I've striven to either be successful in getting compounds to the clinic or ending



them quickly, rather than have them drag on forever."

He counsels other scientists, encouraging thoroughness in preparation before starting on a project.

"It's important to do all of the research up front: the old adage that an hour in the library saves a week in the lab is very true in my experience," he says.

There is a strong causal link between this approach to discovery and Dr. Sliskovic's personal pursuits. A philatelist and coin collector,

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Dr. Sliskovic directs his interest in one country, the stamps and coins of the United Kingdom. He has an almost complete collection of UK stamps, being just four short of a complete collection, and an impressive collection of British coins dating back to the reign of Henry II in the 12th Century. It's a hobby that requires not only an enormous level of knowledge, but also patience and precision.

"I've always considered myself a pretty organized person and with the particular hobbies I have it requires a certain amount of attention to detail, and a preciseness which, in my career, I've tried to achieve at the bench," he says.

Just as important, though is a willingness to take risks in discovery.

Dr. Sliskovic says he worries that despite the enormous hope presented by projects such as the Human Genome Project, there are still very few novel medicines coming out of the laboratory.

"In some respects we're forever plowing the same field, and I would like to see us redouble our efforts in bringing novel mechanisms and novel medicines to the market that have a profound effect on disease as opposed to the slightly better versions of drugs that are already on the market," he says.

To get there will take creativity and a willingness to let scientists follow their instincts and take a risk.

"It's all about being given the opportunity to follow a gut instinct, but we often devalue that trait in people," he says. "Especially in big pharma, companies get very nervous when projects are advanced based on intuition. Smaller companies are a lot more prepared to take that chance. There's nothing wrong with serendipity." ♦

BENCH TO DISCOVERY

DR. BOB SLISKOVIC — RESUMÉ

Feb. 2008 — Present. Director, International Discovery Sourcing Consultants (IDSC), Chelsea, Mich.

2005 — 2007. Senior Director, Pfizer Inc., Ann Arbor, Mich.

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EDUCATION

1979 — 1982. Doctor of Philosophy in Chemistry, University of Keele, Keele, United Kingdom

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