Making new medicines is the most complex team sport on earth. It involves a group of people coming together and practicing as an effective team time and time again.

Millennium Pharmaceutical's JOSEPH B. BOLEN, PH.D. Discusses Advancements in Oncology Research

Throughout his career, Joseph Bolen, Ph.D., has been involved in unraveling the mysteries of drug discovery. Now in his positions as Senior VP of Research and Drug Discovery, a role in which he heads all biological research and related functions as well as all drug-discovery functions, and as Chief Scientific Officer of Millennium Pharmaceuticals he is sharing his vast wealth of knowledge and expertise.

CAREER Highlights

Joseph Bolen, Ph.D., has been Chief Scientific Officer of Millennium since 2006, having joined the company in 1999 as VP of Oncology. He was promoted to Senior VP of Discovery Research in 2002 and appointed Senior VP of Research and Drug Discovery in 2003. Before joining Millennium, Dr. Bolen was VP of Oncologic Diseases at Hoechst Marion Roussel. Dr. Bolen has served as Chief of the Biochemical Oncology Section of the National Cancer Institute. He received the National Institutes of Health Award for Meritorious Research in 1990 for his key contributions to the discovery of the normal physiologic functions of the src group of protein tyrosine kinase oncogenes as key regulators of the immune system.

It's a very interesting and exciting time in the field of oncology, particularly in the area of drug discovery. For Dr. Bolen and his colleagues and peers in the oncology arena, there is a sense of gratification as the time and effort of worldwide cancer research efforts over the past 25 years are finally starting to yield results.

Dr. Bolen recently chaired IBC's 12th Annual World Congress on Drug, Discovery & Development of Innovative Therapeutics conference in Boston, where he also moderated a panel discussion on the topic "Why is Cancer Drug Discovery so Difficult."

We are honored to have Dr. Bolen provide his insights on this exciting area of research in an exclusive interview with PharmaVOICE.

GENOMIC INFLUENCES

What are the most exciting aspects of drug discovery and research in oncology?

BOLEN: The whole era of genomics has had a major impact and we're just starting to see the fruits of this area of research. When I started out, the only tools we had were cancer-causing viruses in animals. We've progressed a long way. We now have major insights in terms of dissecting and understanding the molecular nature of cancer and the broad complexity of specific cancers.

MILLENNIUM'S Approach

With the discovery and approval of Velcade, which is indicated for the treatment of patients with multiple myeloma who have received at least one prior therapy, Millennium has helped to pioneer a new, broad field of biology that is being applied to oncology, and that's the field of protein homeostasis. This is the understanding, at the post-translational level, of how cells balance protein levels. One key pathway used by all cells to regulate protein levels is the ubiquitin proteasome pathway or UPP. The last step on this pathway is the proteasome. Proteasomes are enzyme complexes present in all cells that degrade intracellular proteins in a regulated manner in both healthy and cancerous cells. Cancer cells depend on proteins regulated by the UPP for proliferation and survival. Inhibition of the proteasome by Velcade prevents degradation of intracellular proteins, affecting multiple signaling cascades within cells. This disruption of signalling pathways in the cancer cells can lead to cell death and inhibit tumor growth.

OVERCOMING BARRIERS

What have been the major stumbling blocks in cancer drug discovery?

BOLEN: With any type of cancer, there is an enormous heterogeneity from patient to patient, even with the same type of cancer. The types of cancers we're routinely evaluating in clinical trials are metastatic cancers that have survived numerous rounds of therapeutic intervention. These are cancer phenotypes that have been selected not only for their internal capability to survive, grow, and induce new blood supplies (through the process known as of angiogenesis), but they are also treatment resistant.

If this is not enough of a challenge, we must cope with one of the hallmarks of cancer — genomic aneuploidy, which means that these cells contain not single genomes but rather larger scramble genomes allowing for more rapid stress adaptation. Thus, we have to deal with a massive number of shifts in the disease over the course of time, even in an individual patient and in an individual cancer type, so it's no wonder this is such a complex arena to try to address in the research and discovery phase of drug development.

ADVANCING DRUG DISCOVERY

How have research scientists been able to advance oncology drug discovery?

BOLEN: With the tools that are now available — genomics, proteomics, and other wonderful advancements that have come to be in the past few years — we are more optimistic than ever that we will be able to define the various biochemical pathways that drive the course of the disease. And once this is accomplished, I think that collectively, as an industry of drug hunters, we're going to be able to do something about changing the course of cancer treatments and provide effective treatment options for our patients.

Already, this research has resulted in the emergence of many new targeted therapeutics, with the poster child being Gleevec. We're also learning more about how targeted therapeutics can be combined in the clinic to manage specific subtypes of cancer.

Because there are so many new discoveries coming out year after year, I'm more optimistic about the future of cancer drug discovery and development than ever, and I'm a pretty optimistic guy.

CREATING INNOVATIVE MEDICINES

What are your thoughts on innovation in the industry?

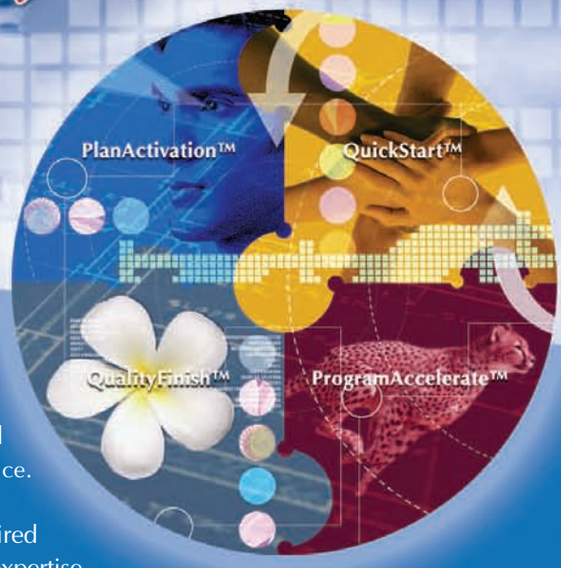
BOLEN: I believe the industry forgot what it really takes to make innovative medicines and did not invest appropriately in discovery. It's not that we didn't spend money on technology and instruments, but in the 1990s somebody came up with the idea that drug discovery was an engineering problem, and nothing could be further from the truth. Making new medicines is the most complex team sport on earth. It involves a group of people coming together, practicing as an effective team and engaging in multidimensional problem-solving in real time. The most important thing about drug discovery is the culture of the organization. If drug discovery was only a numbers game — screening many compounds against many targets by one group and following up with passing things along to another group doing another thing passing it along yet again to some other group to do something else, then presumably the largest companies with the most compounds and the most people would win every time, but that's not the case. It is a fine way to build a car but a poor way to craft a potential new medicine. Success in crafting new drugs is about creating a culture of innovation and allowing creativity to take over at the appropriate time. ✦

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

We've Expanded Our Focus

Adding Infectious Disease Capabilities to Our Global Offering

The Trusted Process™



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To provide the therapeutic depth our customers have come to expect, INC Research acquired Advanced Biologics, a US-based full service CRO that has been industry-recognized for its expertise in infectious disease research.

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