Dr. Bell has been at the forefront of changing attitudes toward rare and ultra-rare diseases around the world.

Alexion's **DR. LEONARD BELL**

Strikes a High Note for Ultra-Rare Disease Development

Dr. Leonard Bell, CEO of Alexion Pharmaceuticals talks about the challenges, opportunities, and changes he has witnessed in the area of ultra-rare diseases, and how there is greater hope for patients, their caregivers, and companies eager to enter the field.

In 2007, Alexion received FDA and EU marketing approvals for Soliris, a first-in-class complement inhibitor, as a treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH), an ultra-rare debilitating and life-threatening blood disorder. In working with ultra-rare diseases, Dr. Bell discusses the different opportunities and challenges compared with more mainstream conditions.

RARE OPPORTUNITIES AND HURDLES

What are the opportunities and challenges associated with rare or ultra-rare diseases?

BELL: I perceive four major opportunities in rare disease. These are heightened in conditions that affect fewer than 20 patients per million and thus are actually ultra-rare. The first, and this is reconfirmed for me every day, is that there's a tremendous opportunity to help individual patients who have been left behind by their healthcare systems, largely because there's generally very little understanding of their disorder, and few, if any, treatments. Secondly, from a scientific perspective, we can develop a detailed understanding of a disease and uncover scientific explanations in areas where there typically has been very little research performed. Thirdly, as we begin to understand the complex mechanisms that are in play in patients with an ultra-rare disease, often we gain insights that help patients who have other rare diseases. For example, we are developing an increasingly strong understanding of the science underlying the pulmonary hypertension, kidney disease, blood clots, severe abdominal pain, and fatigue that afflicts patients with PNH. As we gain this knowledge, we realize that it is important to evaluate Soliris, a first-in-class complement inhibitor, in patients with other rare, complement-mediated diseases who suffer from some of these same morbidities. The fourth opportunity is commercially aligning the prospects for improving care for every individual patient with the performance of the company.

As with the opportunities, the development challenges we face with rare and ultra-rare diseases are similar to those for other diseases, but often amplified. These challenges fall into three main categories. First, in many rare diseases, there's a small body of scientific research and an even smaller body of existing clinical research, which makes it initially difficult to understand the parameters and background of the disease. Secondly, because the disease is ultra-rare, it's difficult to obtain access to enough patients for a trial and to assemble an international team of investigators. The last challenge is explaining the science to regulatory authorities — in parallel and across multiple jurisdictions — who typically have limited, or more likely, no experience with the disease. Given these and other challenges, it is no wonder that rare and ultra-rare diseases have come to be been labeled as "orphan" or "ultra-orphan" disorders.

A COMMERCIAL PERSPECTIVE

Having received marketing approval last year for Soliris to treat PNH in the United States and Europe, what are some of the complexities involved with commercializing ultra-rare disease treatments?

BELL: One of the biggest challenges is educating physicians and identifying patients who can benefit from Soliris. It's important to help physicians correctly diagnose those patients, because in ultra-rare diseases usually a large percentage of people are undiagnosed. Another commercial challenge is working with private payers, mostly in the United States, and national healthcare systems, typically outside of the United States, to explain the value of the therapy and the need for patient access for a disease that the payer has never heard of. Add to that the complexity of having to understand in detail the often-substantial differences in the healthcare delivery systems across 30 to 40 countries. Since we've stated our objective of providing access to all patients who may benefit from treatment, we need to try to make provisions for individuals who are left behind by their healthcare system.

ACADEMIC CONNECTIONS

How can academic researchers and drug development researchers work together for optimal results?

BELL: Researchers at an innovator biopharmaceutical company such as Alexion typically focus on a narrow scientific area and commit enormous amounts of human and financial resources to understand the implications of a disease as rapidly as possible. Because of a relative scarcity of funding, academic researchers typically have fewer resources and therefore are less able to focus as effectively on a narrow scientific area. Also, they are usually far less time-driven than scientists on the development side. On a clinical basis, biopharmaceutical company researchers bring a highly focused and experienced effort that takes into account regulatory implications, how to execute a clinical trial, and how to design a trial with the outcome in mind — that is, ensuring that a drug will have a meaningful impact on a patient's life. Academic researchers bring the intuitive and empiric knowledge of their individual patients and a lifetime of experience in caring for a patient population. So these can be very fruitful collaborations; we take that academic understanding and turn it into something productive and clinically meaningful for patients.

A WORLD OF CHANGE

What are the most significant changes you've witnessed in the ultra-rare disease arena since founding Alexion?

BELL: The changes that have occurred in the development of biopharmaceuticals have been striking for patients with rare diseases. For one thing, there's a greater understanding that it's vital for these patients to have access to therapies. This is a result in part of the passage of the Orphan Drug Act and the societal implications of leaving no patient behind. This wasn't necessarily appreciated 15 to 20 years ago. Increasingly governments, particularly in Europe, are focusing on patients with rare diseases. Alexion has been at the forefront of this movement, and the changing attitude provides incentive for other companies to follow. Start-up companies are now forming to help patients with rare diseases, and patient advocacy groups are assembling and rallying around the world. ✦

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

CAREER Highlights

Leonard Bell, M.D., CEO of Alexion, is also the Principal Founder of the biopharmaceutical company, which was established in 1992. From 1991 to 1992, Dr. Bell was Codirector of the Program in Vascular Biology at the Yale University School of Medicine, where starting in 1990 he had also been an Assistant Professor of Medicine and Pathology in the Department of Internal Medicine; he was also an attending physician at the Yale-New Haven Hospital from 1990 to 1992. Dr. Bell received the Physician Scientist Award from the National Institutes of Health and Grant-in-Aid from the American Heart Association. He also has received various honors and awards from academic and professional organizations. Dr. Bell was a director of The Medicines Company from May 2000 until April 2005, and he served as a director of the Biotechnology Research and Development Corp. from 1993 to 1997.