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エピザイムの挑戦

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Transforming Cancer Therapy via HMT Inhibition

Robert Gould, Ph.D., President and CEO, and Jason Rhodes, Executive Vice President and Chief Business Officer, Epizyme

Epizyme, a Cambridge-based biopharmaceutical company focused on developing innovative drugs based on discoveries in the field of Epigenetics, has recently attracted significant attention for its work in cancer research. We spoke with Robert Gould, President and CEO, and Jason Rhodes, Executive Vice President and Chief Business Officer, about the company's intellectual property and the challenges involved in developing histone methyltransferase (HMT) inhibitors.

Please describe the significance of the intellectual property you have licensed from Dr. Zhang of the University of North Carolina.

Gould: Dr. Zhang's intellectual property is based on his seminal observations on the biochemistry of the enzymes that modify chromatin. It deals with the key focus of our company, the histone methyltransferase enzyme family, but it is a much larger estate than that. His intellectual property provided the underpinnings that enabled Epizyme to be founded in late 2007, and facilitated our \$14 million Series A financing in early 2008. Without his intellectual property, it would have been difficult to obtain the financing and, more importantly, impossible to understand why these enzymes are so critical to human disease, including cancer. Since then, we have been creating our own intellectual property that focuses on small molecule inhibitors for the histone methyltransferase family. We also have significant trade secrets around our drug discovery platform.

What are some of the challenges involved in developing histone methyltransferase inhibitors? Conversely, what are some of the characteristics of this target class that make it attractive for drug discovery?

Gould: This target class is a brand new space in drug discovery. There are no known inhibitors of this class of enzymes. This, of course, poses the typical kinds of challenges that one faces when trying to move into a new space, particularly in drug discovery. Secondly, our research strategy—which is to leverage our understanding of the human genome to enable us to focus on those enzymes that are particularly important in human disease—requires an expertise in identifying which histone methyltransferase enzymes

are relevant, particularly to oncology. Having identified these relevant targets, our aim is to develop specific and precise biochemical and cell-based assays, as well as animal models, that enable us to move the drug discovery programs forward.

In some ways, these challenges are typical for any company that is at the leading edge of a new area of biology, in the sense that we are making discoveries as we go along. However, these challenges also make it such an attractive class of targets for us for drug discovery. It has become clear through efforts to sequence cancer genomes that the members of this family of enzymes are critical in the development of certain cancers, such as leukemia. It is also clear that these enzymes are amenable to small molecule inhibitors. This has been one of the crucial findings that we have come across since Epizyme was founded, and it is the result of key experiments performed by Dr. Zhang. These two discoveries mean that we have the opportunity to take very targeted molecules forward into differentiated patient populations in which it is clear that the cancers are being driven by underlying genomic changes. We think that these characteristics make it a very attractive target for drug discovery.

Is Epizyme initially focusing just on oncology indications?

Gould: Yes, for right now we are for our in-house, proprietary pipeline, and this is for a couple of reasons. One is that, as we move forward into the 21st century and look for opportunities to create personalized medicine—or to create medicines that are driven by the genome of a particular individual— outside of what Epizyme is doing, large efforts are focused on sequencing cancer genomes. Projects such as the NIH’s initiatives and the initiatives of the National Cancer Institute in the United States, or the efforts of the Sanger Institute in Europe to sequence genomes, have given us a treasure trove of information regarding specific changes occurring in oncology that drive tumor cells.

One of the products of these kinds of analyses of is an awareness that the histone methyltransferase family of enzymes is in a number of cases driving cancer. Because of the solid foundation of scientific work that is emerging through the sponsorship of other research institutes, we decided to focus just on oncology. We believe that this will enable us to conduct focused clinical trials, which we can quickly move forward to proof-of-concept trials, by specifically focusing on patients in whom there is a very specific genetic change, therefore allowing us to work with patients who are most likely to benefit from the kinds of therapies we are developing.

Please describe Epizyme's partnering strategy.

Rhodes: Our business strategy has two elements to it. The first includes programs that we are pursuing ourselves. These are oncology indications where there is a clear genetic linkage between the target enzyme and the disease. In these kinds of diseases, not only is there a significant unmet need, but they are also very tractable for a company of Epizyme's size. At the same time, the HMT space is a fairly large space, and as such, it is a larger space than we can practically pursue on our own. Given this, the broad relevance of our platform, and the recognition on the part of large pharma about the leadership and

expertise that Epizyme possesses in this field, our plan is to enter into a single partnership around several other targets within the broader HMT space.

Profile

Robert Gould, Ph.D.

Mr. Gould joined Epizyme as president and CEO in March, 2010, from the Broad Institute, where he was Director Novel Therapeutics. Prior to this, he held a variety of leadership positions during his 23 years at Merck, where he was instrumental in shepherding more than 20 compounds from discovery into clinical development and market in multiple therapeutic areas. Mr. Gould obtained degrees from Spring Arbor College, Michigan and The University of Iowa and undertook post-doctoral studies at The Johns Hopkins University. He has published over 90 peer-reviewed publications and 16 patents.

Jason P. Rhodes

Mr. Rhodes joined Epizyme in March, 2010, from Alnylam Pharmaceuticals, where he was Vice President of Business Development. At Alnylam Pharmaceuticals, he led transformative partnerships including a landmark \$1 billion partnership with Takeda Pharmaceuticals, the spin out of Regulus Therapeutics, Regulus' \$600 million partnership with GSK, and important product partnerships with Kyowa Hakko Kirin, Cubist, and Roche as well as a broad range of in-licensing. Mr. Rhodes received his BA from Yale University and his MBA from the Wharton School of the University of Pennsylvania.