

SHOW ME THE MONEY

Rare disease companies seeking capital to fund drug development have a growing list of sources to turn to, although their ability to access funding from any of these will depend in part on their stage of development, as well as a host of other variables include timing, position, persistence, and luck.

During a presentation at Global Genes 2015 RARE Patient Advocacy Summit, Alison Silva, principal and co-founder of the consulting firm The Orphan Group, as well as EVP, COO and co-founder of Synlogic, and Bharatt Chowrira, president of Synlogic and a successful biopharmaceutical industry veteran, discussed the different opportunities rare disease drug companies have to gain access to capital.

Though obtaining capital is always a challenge, Silva said the good news is that investors not only see a social benefit to investing in rare disease drug developers, but economic advantages as well. That's because clinical trials for orphan drugs—drugs developed for patient populations of 200,000 patients or fewer in the United States—generally require smaller patient populations and are significantly less expensive to conduct than non-orphan drugs. Late-stage clinical trials costs a median of \$44 million to conduct compared to \$188 million for drugs with non-orphan indications.

Nevertheless, drug companies see bigger returns on investment with orphan drugs, which now account for about 20 percent of global prescription drug sales. The compounded annual growth of the orphan drug market is expected to be nearly twice that of non-orphan drugs between 2014 and 2020 with the top 50 orphan drugs generating sales of \$176 billion in 2020.

Another benefit is that orphan drugs benefit from a variety of regulatory mechanisms that can provide them with a faster development path to market and additional economic incentives. This includes such things as orphan drug designation and breakthrough therapy designation, as well as the rare pediatric priority review voucher. The voucher, which is issued to qualifying rare disease drugs, can be sold. Because it can provide companies with market access for any new drug six months earlier than they would otherwise be able to obtain, it can generate significant monetary value. In August 2015, United Therapeutics sold its voucher to AbbVie for \$350 million.

At the pre-clinical stage, rare disease drug companies can seek to access capital from government grants, such as grants from the National Institutes of Health or Small Business Innovation Research grants among others. NIH devotes about 11 percent or \$3.5 billion of its annual research budget to orphan drug related research, according to Silva. Foundations and disease focused organizations are also a potential source of funding. The good news is that these sources of funding will be non-dilutive, which means that it does not require the sale of the company's shares, and therefore does not cause dilution of the existing shareholders.

Corporate venture arms, venture investment funds run by pharmaceutical and biotechnology companies, may be more willing to take risks since their investments may be driven more by strategic reasons rather than their expectation of a direct financial return on investment. These firms may be using these transactions as a way to build their future pipeline or gain understanding of a therapeutic area or emerging technology. Similarly venture philanthropy—venture arms of philanthropic groups—will take on earlier stage investments and greater risks because of their desire to advance therapies in a specific disease area.

As companies advance therapeutic candidates into the clinic, investors view their risk of success mitigated and they are able to obtain additional sources of capital and larger amounts needed to fund clinical development. While angel investors might be willing to invest in early-stage companies, few venture investors today are interested in doing so. Venture investors, though, will start to become interested when companies can establish proof-of-concept or demonstrate that a disease pathway or mechanisms has the potential to be effective at treating a disease.

An alternative to capital markets is strategic partnerships with pharmaceutical and biotech companies.

In such cases, drug developers will license out a drug for specific markets or globally in exchange for such things as development costs, fees, and royalties. In choosing strategic partners, Silva suggests that companies look for partners

and investors who can provide more than just capital. This might be having a pharmaceutical company with a mouse model or other infrastructure that can save time and money in the drug development process.

After running through the who, what, and why of financing, Silva offered a simple guide to the question of where and when. "Go everywhere," she said, "and ask for it always and often."

CONTENT SPECIALISTS

Bharatt Chowrira, Ph.D., J.D.

Dr. Chowrira joined Synlogic as President in September 2015. Reporting to the CEO, his primary responsibilities include overseeing and managing corporate and business development, alliance management, financial and legal operations. Dr. Chowrira brings a strong track record in the biopharmaceutical industry with more than 20 years of experience, combining a unique blend of research, corporate development, operations, financing, legal and licensing expertise. Dr. Chowrira was most recently the chief operating officer of Auspex Pharmaceuticals which was acquired by Teva Pharmaceuticals in the spring of 2015. Previously, he was president and chief executive officer of Adnex Therapeutics, a biotechnology company publicly-traded on the SIX Swiss Exchange. Prior to that, he held various leadership and management positions at Nektar Therapeutics, Merck & Co., Sirna Therapeutics, (acquired by Merck & Co.) and Ribozyme Pharmaceuticals. Dr. Chowrira received a J.D. from the University of Denver's Sturm College of Law, a Ph.D. in Molecular Biology from the University of Vermont College of Medicine, an M.S. in Molecular Biology from Illinois State University and a B.S. in Microbiology from the University of Agricultural Sciences, Bangalore, India.

Alison Silva, Executive Vice President, Chief Operating Officer and Co-Founder, Synlogic

Alison Silva is EVP, COO and co-founder of Synlogic, a therapeutically-focused synthetic biology company, initially developing therapeutics for inborn errors of metabolism including UCD, PKU and MSUD; with an expanding pipeline into other metabolic disorders, inflammatory disease and oncology. Alison is also the Principal and Co-founder of The Orphan Group, a specialty consulting company focused on assisting companies with their orphan drug development strategy, implementation and lifecycle product management. The Orphan Group employs a consortium of rare disease experts with talents spanning all stages of orphan drug development, in order to provide the required knowledge and expertise to primarily early stage companies in a resource and capital efficient manner. Additionally, The Orphan Group provides corporate and business development capabilities, including extensive search in evaluation efforts, to facilitate collaborations and partnerships in the rare disease industry. Ms. Silva began her career in drug development in clinical operations in various positions at Pfizer, Massachusetts General Hospital and the University of Massachusetts. Alison holds a B.S. in Biology and Mathematics from Clark University, and a M.S. from Clark University and UMass Medical Center.

Session Briefs Summarized by, Daniel Levine

Daniel Levine is an award-winning business journalist who has reported on the life sciences, economic development, and business policy issues throughout his 25-year career. Since 2011, he has served as the lead editor and writer of Burrill Media's acclaimed annual book on the biotech industry and hosts The Burrill Report's weekly podcast. His work has appeared in The New York Times, The Industry Standard, TheStreet.com, and other national publications. He also is the host of RARECast™ podcasts.