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WHY GENETIC MEDICINES AND WHY NOW?

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Thank you, Andrew. It is an honor to be here and to be amidst this august crowd and this celebration of scholarship and indeed humanity in honor of Dr. Markowitz. I don't often write out my comments, but I've got 5 minutes and I'm following Andrew, which is always a daunting task. I've been lucky to have Andrew as a mentor in my life, and I'll have more to say about that at the end. But I wanted to begin by reporting to you from the front lines of the interface between biological sciences, drug R&D, and the marketplace that finances that activity. And I'll offer two quick reports that encapsulate both the promise and the challenge of our current moment.

Report 1 starts with the sequencing of the human genome around the year 2000. Shortly after this, the pharmaceutical industry entered a period of declining R&D returns with the ROIC of R&D well below its WACC. Why? Our hope was that this newly discovered code would tell us more about why and how disease arises. It didn't appear to, at least in a predictive way, for most of the conditions the pharmaceutical industry is focused on—larger diseases like heart failure or asthma because those conditions arise from a large number of diverse genetic and environmental insults. However, beginning in 2005 and beyond, we began to rapidly identify and characterize a class of disease we call monogenic disease. These diseases, otherwise known as Mendelian diseases, are typically inherited diseases like sickle cell or cystic fibrosis. There are, at last count, over 8,000 Mendelian diseases. They affect almost 30 million Americans, tend to be pediatric, and tend to impact patients with devastating consequence—they are the second highest contributor to childhood mortality. But the good news is, the sequencing of the human genome allowed us to characterize these conditions in exquisite detail. For the first time, in many diseases, we could go from genetic insult to cellular dysregulation to 'what does the cell or ECM [extracellular matrix] do wrong' to what's happening at the tissue level to, ultimately, what is happening to a patient. Ever-decreasing costs of sequencing coupled with big databases that link genetic information to phenotype coupled with new drug approaches that target gene products at

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their source meant that, within this class of disease, POTS [probability of technical success] was a remarkable 4 times higher than average drug R&D and ROIC was 2 times higher. However, despite these advantages, there are less than 100 approved therapies in this field of 8,000+ diseases.

Report 2 is even shorter. As many of you know, biotech is just emerging from its 'tech-like bubble' pop. Our index, the XBI, has seen a dramatic turn down—the last time we saw something like this was in the mid 90's and turndown was as severe as what happened to tech in 2001 if not more. A consequence of this has been a flight of capital, in particular in the earliest stages of R&D, the so-called Valley of Death. We start 200 new companies per year, in an industry where biotech is the most important source of new drugs. Consider, however, that the NIH grants 50,000 awards per year, that 1,600+ healthcare patents are generated per year in academia alone, or that 300+ disease causing genes were mapped last year in tandem with the complete human reference genome and the advent of AI-tools like AlphaMissense that allow us to rapidly map mutations to pathogenicity. In the rare and orphan drug world, only 2 companies were started in first half 2023.

The message from these two reports is simple. Profound advances in genetics offer us a universe of disease and patients that can be helped, at high probability and in NPV-positive ways by the way. But the current marketplace, with its emphasis on early stage, dreamy narratives or late stage, me-too blockbusters, in large part misses this opportunity.

At BridgeBio, our aim is to address this opportunity by applying Andrew's theory of diversification coupled with a highly efficient approach to drug R&D. Our de-centralized model allows us to prosecute over 20 programs at any given time, across a wide span of therapeutic areas, prevalence sizes, and modalities. We've raised over $2 billion in capital to do our work, a majority of it away from equity, which has allowed us to provide equity holders with well-above benchmark ROE to date. Our convertible debt was amongst the top performing across the entire market in 2023. And we've put our capital to reasonable use, driving 2 approvals (with another to come this year) and 19 INDs [investigational new drug applications] in approximately 8 years, putting BridgeBio in the top 5 most productive R&D biotech organizations in the last 20 years. Through the ups of being the fastest biotech to a $10 billion market cap to the lows of missing on Phase 3 clinical trials, we have maintained a long-term view focused on patient impact made possible through the unique capital structure that Andrew published on a decade ago.

I'd submit to this audience that we are just getting started. With support from leaders like you in the room, there are many doable problems to work on; many patient lives that can be improved. Now more than ever, in a biotech marketplace that has been shattered in the last 2 years and is now more concentrated and less diverse than ever, we need new business models to address patient unmet need.

I was recently in the UK and had the opportunity to meet a young boy and his family afflicted with a devastating disease called MoCD [molybdenum cofactor deficiency] Type A. Before we developed the only approved drug for this disease, it was a uniform death sentence. But today the boy is, remarkably, meeting typical growth goals. In conversation, the boy's mom asked me why we decided to take on MoCD Type A when no one else would. The question wasn't so much why—a thriving, living boy who will hopefully go on to live a productive life gave me all the answer I need—the question was how. And the answer to that is Andrew Lo and portfolio theory applied to biotech. Thank you for the time and I'll pass it back to Andrew.