

Bridging the Valley of Death through Financial Innovation

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Prepared for the U.S. House of Representatives

Financial Services Committee

September 11, 2019

Good morning, Chairwoman Waters, Ranking Member McHenry, Chair Maloney and Ranking Member Huizenga, and members of the committee. Thank you for giving me this opportunity to testify today, and for this committee's commendable track record of attending to the important financial issues of the day and bringing legislation to bear towards their solution.

Promoting Innovation Through Increased Access to Capital

The American economy is the largest single engine of innovation the world has ever seen. For over two centuries, entrepreneurs from all over the world have launched small startups in this country to try out and test new ideas and inventions in the American marketplace, from the workshops of New England to the garages of what we now call Silicon Valley. These startups have been an incredibly important source of innovation. For example, the telephone, the light bulb, and the personal computer are all products of this combination of ingenuity and entrepreneurship.

The innovation cycle is vitally important to the economy of goods and services, what is sometimes called the "real" economy. However, fostering growth in the innovation cycle requires investment, and this investment comes from the financial economy. The key driver

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of this cycle is access to capital, and the common theme among the pieces of legislation before this committee today is improving access to capital.

Without capital, a potentially useful new idea will remain just that—an idea. It may require further refinement or development or testing before it can be brought to market. It will almost always require more resources to reach commercial production. As a result, in the modern American economy, angel investors and venture capital are essential ingredients of growth and innovation. They supply the necessary capital to move an idea from the garage and the laboratory to consumers and patients. Venture capital in U.S.-based startups surpassed \$130 billion in 2018,¹ and anything that allows for better access to capital is fundamental to accelerating innovation.

However, “better access to capital” is not always synonymous with “more access to capital.” Innovation is inherently risky, and despite the possibility of high reward, not all investors are willing or able to take certain risks. To reduce the likelihood and severity of unintended consequences such as panic-selling, market crashes, and financial instability, investors shouldn’t be investing in assets they don’t understand and shouldn’t be taking risks they’re not able to tolerate.

This is precisely the motivation for the important concepts of “suitability,” “accredited investor,” and “fiduciary duty” in securities regulation. For example, the Financial Industry Regulatory Authority mandates through its Rule 2111 that investment professionals take into account a customer’s financial situation, their investment experience, and their risk tolerance before making a recommendation.² They have a professional responsibility—and in many cases, a fiduciary duty—to make sure that the investments are suitable for the investor. Even if it does not apply in every circumstance, we should consider the spirit of financial suitability and fiduciary duty in our legislative framework.

Adjusting the Regulatory Balance

In 1982, the U.S. Securities and Exchange Commission (SEC) adopted Regulation D to adjust the balance between the protection of investors and the formation of useful capital, especially for small businesses.³ It did so by creating commonsense classes of exemptions to the earlier Depression-era requirements for securities offerings originally adopted by the SEC. The reasoning behind these exemptions was simple: lowering the registration requirements of a company’s offering under Regulation D would increase its access to capital, but larger offerings would be available only to “sophisticated” and accredited investors, who would be better equipped to understand the more complex risks involved. Lawmakers struck a balance between unrestrained capitalism, “red in tooth and claw,” and overregulation, imposing disproportionate costs on entrepreneurs.

¹ PitchBook (2019).

² FINRA (2014).

³ 17 C.F.R. §230.501 et seq.

The exemptions of Regulation D are fully in the spirit of financial suitability. An accredited investor is broadly defined by the SEC to include financial institutions, benefit plans, charities with a significant amount of assets, and so on, as well as investors above a certain net-worth or income level. These are either entities run by financial professionals, who are aware of the risks, or individuals who can afford to take larger risks in their financial investments.

The Family Office Technical Correction Act,⁴ sponsored by Rep. Maloney in the 115th Congress, and the Fair Investment Opportunities for Professional Experts Act,⁵ sponsored by Rep. Schweikert and eleven of his colleagues in the 115th Congress, are commonsense expansions of those exemptions. The Family Office Technical Correction Act would include family offices in the definition of accredited investor in Regulation D, where a family office is a private investment company that only serves family clients, who typically have high net worth. The Fair Investment Opportunities for Professional Experts Act would do the same thing for licensed brokers and investment advisors.

Regulation D has been revised several times since its inception, precisely because it is such a powerful piece of legislation. Perhaps future generations of policymakers and regulators will think even more broadly of the concept of the “accredited investor.” Instead of high net-worth individuals automatically being classified as accredited investors, one can imagine basing the definition on specific educational prerequisites.

We already impose educational requirements in a variety of professions. Drivers must demonstrate proficiency in a written and road test before they are awarded a license to operate a motor vehicle. Truck drivers must undergo even more extensive training and testing before being allowed to operate an 18-wheeler. Similar requirements can be found in virtually every profession and activity involving significant risk and skill: becoming a firefighter, police officer, or an emergency medical technician, or purchasing and operating firearms, ham radios, and motorcycles. Shouldn't investing one's entire retirement assets also be considered sufficiently risky and requiring necessary skills to warrant specialized training and licensing?

A broadening of the accredited investor pool through changes in Regulation D to include family offices and professional experts would allow these investors to participate in private offerings. In the same vein, market innovations like crowdfunded vehicles and venture exchanges would allow small and speculative enterprises to reach a greater number of investors. The Crowdfunding Amendments Act,⁶ sponsored by Representatives McHenry and Waters in the 115th Congress, and the Main Street Growth Act,⁷ sponsored by Representatives Emmer and Gonzalez in the 116th Congress are intended to allow exactly that.

⁴ H.R.3972 - Family Office Technical Correction Act of 2017.

⁵ H.R.1585 - Fair Investment Opportunities for Professional Experts Act.

⁶ H.R.6380 - Crowdfunding Amendments Act.

⁷ H.R.2899 - Main Street Growth Act.

The Crowdfunding Amendments Act expands the criteria to allow a crowdfunding issuer to sell shares through a crowdfunding investment vehicle. Crowdfunding is a natural financial consequence of the great wave of technological innovation that created the Internet, through which individuals are able to pool even very small amounts of money to support specific goals and enterprises. While the aggregate amounts of money raised through equity crowdfunding so far are small (only \$300 million in its first year as a recognized category of securities offering), the firms using crowdfunding have exceeded their targeted offering amount by 300%, implying significant excess demand.⁸

Venture exchanges, as endorsed in the Main Street Growth Act, are another innovation that allows smaller and more speculative enterprises greater access to investors. The idea is simple: to create an exchange with fewer listing requirements than one of the larger, more traditional exchanges, but with greater structure than the current over-the-counter markets, specifically for companies with big ideas but small capitalization. Venture exchanges are not an unproven idea. Canada has had a national venture exchange since 2001, which allows many small Canadian natural resources companies to reach interested investors. In the United States, it is hoped that similar exchanges will allow small technology companies with early-stage concepts in development to gain greater access to capital.

However, the effects of these innovations should be monitored. Right now, the markets are migrating away from traditional public offerings of securities towards private and quasi-private offerings. One commonly cited reason has to do with the fact that organized exchanges aggregate all known information about a company and incorporate it into the price of the company's stock, through a process that the financial writer James Surowiecki has called "the wisdom of crowds." However, the price of an initial public offering can be a surprise to its issuers, sometimes welcome, sometimes not. Many companies are believed to be moving away from public offerings because of this element of surprise. Nevertheless, the possibility of surprise is widely thought to be a crucial part of the price discovery process, which is essential for a well-functioning market.

What does this shift away from public offerings imply for newly listed companies? Right now, the evidence is unclear. The Private Securities Transparency and Reform Act of 2019 and the as-yet-unnamed act on the effects of private securities offerings are meant to fill this informational gap. The Private Securities Transparency and Reform Act is explicitly intended to identify the connection between the increase in private and quasi-private securities offerings, and the declining number of initial public offerings. This will require a considerable amount of data collection regarding the characteristics of these companies and their investors. Like a census, this data will be an invaluable guide to policymakers for the purpose of crafting better legislation—one cannot manage what one does not measure. The as-yet-unnamed act will require the SEC to submit a report to Congress about the impact that

⁸ Abate (2018).

any legislative change will have on these private offerings, at which point more targeted policies may be formulated.

The Rare Disease Fund Act of 2019

The proposed pieces of legislation I have commented on so far are intended to allow innovative companies to gain greater access to investors who are comfortable with the higher risks (and higher rewards) of private investments. They allow the financial economy to provide the right kind of capital to the real economy, to create a greater range of goods and services and technologies. However, there is at least one type of innovation that is not as well funded, due to less attractive risk/reward profiles: early-stage biomedical innovation.

The range of medical treatments available today is more advanced than ever before. However, it is not a field where breakthroughs come easily. Any promising result in the laboratory must go through a difficult development process, one that exists not because of onerous regulation, but because it is simply scientifically very hard to do. Translating a promising drug candidate from the laboratory to final approval by the U.S. Food and Drug Administration (FDA) is estimated to cost \$2.6 billion as of 2019,⁹ and for every candidate that makes it, many are left by the wayside. In the field of cancer therapeutics, as of the first quarter of 2019, the current historical probability of success is 4.3%, or a little over one in twenty-five.¹⁰ These are grim odds for everyone involved, including the investor.

In the biopharma industry, this challenge is often captured by the term, “the Valley of Death,” which refers specifically to the difficult path from fundamental scientific investigation to phase 1 and phase 2 clinical trials, which determine the initial safety and efficacy of a treatment.¹¹ This valley is, in fact, an ever-widening gap, separating the basic research so ably performed by our universities and academic medical institutions from the development of new clinical therapies and technologies so badly needed by the patient population. This gap is not caused by a lack of knowledge, but by a lack of funding. There are not enough private investors whose appetite for risk is large enough that they will fund the necessary early-stage research to bring these new treatments and technologies from the laboratory into the clinics for formal medical testing.

However, there are potential solutions. While any given candidate treatment may be a long shot, the odds of at least one success can be greatly increased by bundling enough long shots together.¹² For example, if a single candidate has only a 5% chance of success, the

⁹ See <https://www.policymed.com/2014/12/a-tough-road-cost-to-develop-one-new-drug-is-26-billion-approval-rate-for-drugs-entering-clinical-de.html>.

¹⁰ See <https://projectalpha.mit.edu/>.

¹¹ Medical device manufacturers face yet another Valley of Death, even after receiving FDA approval, in the form of additional tests, design changes, and other costs imposed by Medicare before a device is adopted for use by a wide patient population.

¹² Hull, Lo, and Stein (2019).

chances of at least one success out of a portfolio of 100 statistically independent candidates is 99.4%, close to a statistical sure thing. This is the same principle that a mutual fund uses when it diversifies its portfolio to reduce its overall financial risk. Now imagine a financial structure in which a large number of biomedical projects are funded by a single financial entity. Each project might individually be a long shot, but enough of them pooled together can raise the chance of success to something that even an institutional investor with little appetite for risky early-stage projects might be willing to fund.

Several years ago, my co-authors and I proposed creating these large diversified portfolios of biomedical development projects, which we called “megafunds.”¹³ Our original intent was to develop new business and financing models to accelerate cancer drug development—cancer has likely touched the lives of most of the people on this committee, as indeed it has touched mine. A cancer megafund would be truly mega, requiring billions to have a material impact on patients’ lives, and seemingly too large for the current levels of traditional venture capital. However, the large number of projects lowers the probability of overall failure to a level comparable to high-grade corporate bond defaults, less than one percent. As a result, the financing for the megafund could be structured not as equity alone, but as a combination of equity and collateralized debt.

Debt markets are much larger than the equity markets on which the biomedical sector has traditionally depended. The issuance of debt dramatically increases the potential funding sources for a megafund. By creating a large, diversified portfolio of projects, the megafund lowers the financial risk of biomedical research to the point where institutional funds with conservative investors would find bonds collateralized with the results of its R&D efforts as suitable for investment.

However, it turns out that developing effective cancer therapeutics is one of the riskiest types of drug development at present. Many classes of disease have significantly higher success rates for developing effective therapeutics. Although the basic principle behind the megafund remains the same, the required amounts of capital can be lower for those disease types with higher success rates.

This brings me to the Rare Disease Fund Act, introduced to Congress by Representatives Juan Vargas and Scott Peters. Rare diseases have a formal legal definition in the United States:¹⁴ any disease that affects fewer than 200,000 people in the United States is defined to be “rare.” These diseases include hemophilia, cystic fibrosis, amyotrophic lateral sclerosis (ALS, or Lou Gehrig’s disease), Duchenne muscular dystrophy, the pediatric cancers, and many other genetic and inherited disorders. Although any single rare disease affects only a relatively small number of patients, it is estimated that there are over 7,000 rare diseases, affecting as many as 30 million Americans in total, more than the estimated

¹³ Fernandez et al. (2012), Fagnan et al. (2013).

¹⁴ National Institutes of Health (2017).

number of Americans with cancer.¹⁵ As a group, rare diseases are as prevalent as diabetes among Americans, but some have a much poorer long-term prognosis, and many are fatal. Moreover, the number of rare diseases is likely to grow over the next decade as medical researchers learn more about the origin of disease, and as they use genomics, proteomics, and the other “omics” to stratify patients into smaller sub-categories. Rare diseases are one of the largest unmet medical needs in the country. Yet prior to the 1980s, they were grossly underserved by clinical research because the small patient subpopulations implied that the cost of developing a treatment was unlikely to be met from sales.

This grim financial logic was the motivation for the Orphan Drug Act (ODA) that Congress enacted in 1983.¹⁶ The ODA put into place various incentives for companies to develop drugs for these diseases, such as market exclusivity, tax benefits, and fast-tracked FDA approval. These incentives worked. Since the passage of the act, several hundred orphan drugs have been developed, making it one of the most successful public-policy initiatives in recent years. Some of these treatments are literally miraculous. For example, the gene therapy Luxturna is a cure for a certain type of blindness known as Leber’s congenital amaurosis (LCA), an inherited condition causing retinal dysfunction in infants.¹⁷ Another gene therapy, currently being reviewed by the FDA, treats a condition known as AADC deficiency, which prevents infants and toddlers from developing key motor functions like raising their heads, rolling over, sitting up, and walking.¹⁸ After a one-time treatment of this gene therapy, these patients are able to recover significant motor functions, including the ability to sit up, stand, and even learn to walk.¹⁹ “The blind shall see and the lame shall walk” is a phrase usually associated with religious experiences, but is now a reality thanks to recent breakthroughs by the biopharma industry.

Part of the success in developing rare-disease drugs is the fact that the biological mechanisms responsible for these diseases are typically better understood, often because they have lethal consequences that are traceable to physiological roots (organ failure due to a build-up of certain toxins, the inability to produce certain critical proteins, etc.). And once scientists understand the mechanism for disease, they can begin to develop ways to deal with it. For example, the underlying cause for AADC deficiency is mutations in a single gene that prevents the patient’s brain from producing important neurotransmitters such as dopamine and serotonin. Once this gene was identified, scientists were able to devise an ingenious method for replacing the mutated gene with the correct version so as to restore the ability of the brain to produce these neurotransmitters.²⁰

¹⁵ See <https://rarediseases.org/>. As of 2016, an estimated 15,338,988 Americans were living with some form of cancer according to <https://seer.cancer.gov/statfacts/html/all.html>.

¹⁶ Public Law 97-414.

¹⁷ FDA (2017).

¹⁸ Das, Huang, and Lo (2019).

¹⁹ Hwu et al. (2012), Kojima et al. (2019).

²⁰ Ibid.

Detailed knowledge of disease mechanisms can sometimes be used to “orphanize” more common diseases. For example, the breast cancer drug Herceptin was approved under the ODA as an orphan drug, despite the fact that breast cancer is by no means a rare disease.²¹ But because Herceptin targets a very specific biological mechanism that only a smaller subpopulation of breast cancer patients exhibit,²² it is covered by the ODA which gives the biopharma industry additional incentives to direct their limited resources to these efforts. And as is often the case in biomedicine, a “virtuous cycle” in which success begets more successes can be triggered by an initial drug approval—even for a small patient population—by confirming the validity of the scientific basis for the drug, by generating profits that will partly be plowed back into additional R&D, by raising awareness of the disease through the new drug’s marketing and distribution activities, and by giving new hope to patients and their advocates.

For example, in January 2012, the first drug to treat the root causes of cystic fibrosis (CF), Kalydeco, was approved by the FDA. It was designed by Vertex Pharmaceuticals in collaboration with the Cystic Fibrosis Foundation²³ for an ultra-rare form of the disease that affects only about 4% of all CF patients, not an unqualified success from the total CF patient population perspective. However, this one success demonstrated the feasibility of treating CF by targeting a specific defective protein (CFTR), which encouraged scientists at Vertex to continue along these research directions. These efforts ultimately led to the approval in July 2015 of the two-drug combination Orkambi, which treats a third of all CF patients. And in March 2019, Vertex announced a three-drug combination that successfully met its Phase 3 endpoints;²⁴ if approved, this new drug will have the potential to treat 90% of all CF patients.

This “divide and conquer” approach—stratifying patient populations into smaller groups that have certain biological mechanisms in common, developing targeted therapies to treat one small group, and then building on that success to develop related therapies that apply to other groups—may well be the best strategy for dealing with much more common and less well-understood diseases like Alzheimer’s, dementia, chronic pain, and so on. For this reason, a comprehensive plan for developing rare disease therapeutics should be a national priority.

Using rare disease statistics derived from industry sources, and in collaboration with researchers at the National Center for Advancing Translational Sciences²⁵—a division of the

²¹ In 2019, an estimated 268,600 new breast cancer cases will be diagnosed in women in the U.S., and an estimated 41,760 women will die from it (<https://www.cancer.org/cancer/breast-cancer/about/how-common-is-breast-cancer.html>).

²² Herceptin treats those patients with a specific mutation in the HER2 gene, and this subpopulation is small enough to qualify as a rare disease under the ODA.

²³ See Kim and Lo (2019) for details on how venture philanthropy played a central role in developing CF drugs.

²⁴ Vertex Pharmaceuticals (2019).

²⁵ “The National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health (NIH) was officially established in fiscal year 2012 to transform the translational science process so that new

National Institutes of Health mandated to help bridge the Valley of Death in biomedicine—a group of researchers at MIT (including myself) decided to simulate a megafund for developing treatments for rare diseases.²⁶ Specifically, we investigated two financing techniques: the use of portfolio diversification to reduce risk, and given the reduction in risk, the use of debt financing to increase the potential sources of capital available to the fund, thus improving the attractiveness of returns to equity holders. Surprisingly enough, it turned out that a successful rare disease megafund could be implemented with as little as \$400 million in capital, and in most cases, the simulated returns were even more attractive than the returns of top-performing hedge funds.

Our analysis inspired Dr. Neil Kumar, a biotech venture capitalist, to found the rare disease drug development company BridgeBio Pharma.²⁷ This company applied the first innovation proposed in our paper—the portfolio diversification concept—to assemble a robust pipeline of rare disease drug candidates, mostly from preclinical stages of development, and in less than five years, has brought three therapeutic candidates into phase 3 clinical trials.²⁸ Not only is BridgeBio proving to be a humanitarian and scientific success, the company also shows that the portfolio-theory approach of the megafund is financially sound. In July 2019, BridgeBio held an initial public offering, and now has a market capitalization of just over \$3.5 billion.²⁹ In addition, a recent analysis of the stock market performance of a group of 39 rare disease companies from 2010 to 2015 by my co-author Richard Thakor and me found that the returns of this group far exceeded those of the S&P, NASDAQ, and NYSE/ARCA biotech indexes, respectively, and also outperformed the broad-based S&P 500 index, both in absolute and risk-adjusted terms.³⁰

treatments and cures for disease can be delivered to patients faster. NCATS, one of 27 Institutes and Centers (ICs) at NIH, strives to develop innovations to reduce, remove or bypass costly and time-consuming bottlenecks in the translational research pipeline in an effort to speed the delivery of new drugs, diagnostics and medical devices to patients.” Source: <https://ncats.nih.gov/about/center>.

²⁶ Fagnan et al. (2014)

²⁷ Disclosure: I was a founding investor in BridgeBio and am currently an advisor to the company.

²⁸ One is for an extremely rare inherited disease, molybdenum cofactor deficiency type A. Children born with this deficiency have a median life expectancy of only three years. One is for the inherited disease transthyretin amyloid cardiomyopathy, caused by the buildup of amyloid plaques in the heart, whose only disease-modifying treatment is a heart transplant. The third is for a topical gel meant to reduce the production of basal cell carcinomas in patients who have Gorlin syndrome, a genetic tendency towards having hundreds of these tumors in their lifetimes.

²⁹ As of August 30, 2019.

³⁰ Specifically, from 2010 to 2015, the orphan drug index proposed by Lo and Thakor (2019), referred to as “ORF”, returned 608%, far exceeding the returns of 317%, 320%, and 305% of the S&P, NASDAQ, and NYSE/ARCA Biotech indexes, respectively, and the 83% of the S&P 500. ORF does have higher volatility than the other indexes, but still outperforms even on a risk-adjusted basis, with a Sharpe ratio of 1.24 versus 1.17, 1.14, and 1.05, respectively for the other three biotech indexes, and 0.71 for the S&P 500. However, ORF has a market beta of 1.16, which suggests significant correlation to the aggregate stock market and fewer diversification benefits than traditional pharmaceutical investments. See Lo and Thakor (2019) for details and further analysis.

However, even with these economic and financial incentives, there are still several thousand rare diseases with no FDA-approved therapies, despite the fact that we now have the scientific means to treat—and, in some cases, cure—these terrible afflictions. To cite one personal example, I just learned a few months ago that the 26-month-old son of one of my former students has a rare disease called Pitt-Hopkins syndrome, a hereditary condition that means his child will suffer from epileptic seizures, breathing problems, and delayed motor skills, and will probably never develop speech beyond a few simple words. Scientists have already identified the genetic basis of this disease.³¹ There are already several specific hypotheses about how this condition can be treated effectively and even cured, especially if diagnosed and addressed early.³² However, the costs associated with testing these hypotheses means that, in the absence of some type of catalyst to accelerate development of these treatments, my former student's son will not receive the help he desperately needs.

Representatives Vargas and Peters and I believe that a public-private fund focused on rare disease therapeutics could serve as a viable pilot project for further development of the megafund concept. With more innovative financial and business structures, and the already existing close partnership between orphan drug developers and government agencies like the National Center for Advancing Translational Sciences, we can make even greater progress in easing the burden of disease for millions of Americans.

Under the Rare Disease Fund Act, a megafund will be created under the full supervision of the SEC, and will hire a qualified portfolio manager—a professional with both drug development and financial expertise—to acquire the development rights to multiple rare disease therapeutic candidates. These assets may be sold by the fund at any time. If a candidate successfully completes phase 2 of the clinical trial process, which determines if that candidate is clinically effective, it will be sold by the fund to a company that wishes to further develop the drug through phase 3 and possible FDA approval.³³ This sale will almost certainly be at a profit, under the assumption that the phase 2 trial is successful.

The rare disease megafund will be funded not only through equity, as in the case of BridgeBio, but also through the issuance of bonds, the second innovation proposed by our analysis. Debt financing significantly reduces the cost of capital and, therefore, the cost of drug development, particularly in the low interest rate environment we currently enjoy. And lower drug development costs should eventually imply lower drug prices, other things equal, which is especially relevant for these very small-batch/high-fixed-cost therapeutics.

³¹ See, for example, <https://ghr.nlm.nih.gov/condition/pitt-hopkins-syndrome#genes>.

³² See, for example, Pitt Hopkins Research Foundation (2016) and Thaxton et al. (2018).

³³ In some cases, an attractive sale could occur after successful completion of phase 1, especially in cases where efficacy is demonstrated in a properly designed trial. For example, for certain fatal rare pediatric diseases, a single successful phase 1 trial can provide enough information to warrant approval by the FDA because of the risk/reward trade-off of the new treatment. This type of outcome is particularly relevant for gene therapies, which, in the few cases that have been reviewed by the FDA so far, seem to yield remarkable patient responses for several devastating diseases.

One class of these bonds will be guaranteed by the United States, for a fair-market fee set by the SEC, with the goal of making the guarantee budget-neutral to U.S. taxpayers. This guarantee is intended to make this one class of bonds more attractive to traditional institutional investors. However, non-guaranteed bond classes would also appeal to a large pool of investors such as pension funds and insurance companies, for which megafund bonds would serve as a hedge against longevity and reimbursement risk.³⁴

To avoid any potential misperception of an “implicit” government guarantee for any other securities issued by this megafund, the megafund as a whole, its equity, and its other classes of debt will explicitly *not* have any such guarantee.³⁵ Only accredited investors will be allowed to purchase these securities. Once all the stock is issued, the government will have no further ownership stake in the megafund—the fund will essentially privatize itself.

Because the goal of this legislation is to catalyze private markets to finance early-stage drug discovery and development—not to have government substitute for private markets—the proposed legislation is only intended to guarantee one class of debt of a single megafund. Once this class of debt has been repaid, a sunset provision eliminates any further guarantees, shifting the funding incentives entirely to private markets.

A rare disease megafund with a sufficiently large number of candidates in its portfolio is statistically likely to include at least one promising candidate for phase 3 clinical trials, and perhaps even several. From a purely financial perspective, this would be worth doing even if no greater goal were in mind. However, once this class of funds is established, other groups and consortiums will be able to emulate this megafund for other types of disease—or even for other rare diseases, since there are over 7,000 of them. As investors become more familiar with the megafund concept, more capital will become available for early-stage biomedical research, leading to larger megafunds for more intractable types of disease, such as cancer, Alzheimer’s, dementia, and the many other diseases associated with aging. The megafund model is even applicable to other types of early-stage technological innovation, for example, fusion energy, new energy storage technologies, geoengineering methods to mitigate the thermal effects of greenhouse gases, and so on.

Conclusion

To increase innovation in the real economy, we will need further innovation in the financial economy so as to get the right amount of capital to the right projects with the right investors. Nowhere is this more important than in biomedical innovation and the development of new medical treatments and therapeutics. Already the ODA has had an enormously positive impact on patients with rare diseases and their families. We should

³⁴ See, for example, Stein (2016) and Koijen and Van Nieuwerburgh (2018).

³⁵ Moreover, despite the guarantee for the single class of debt, all of the megafund’s securities—including the guaranteed class of bonds—will be treated under U.S. securities law as neither issued nor guaranteed by the government, hence none of the megafund’s securities will be considered “government securities.”

double down on its success by opening up the floodgates of capital to the very earliest stages of biomedical innovation. The Rare Disease Fund Act would establish a megafund prototype to channel more resources into the “Valley of Death” and transform it into more verdant pastures of biomedical innovation. More capital implies not only a larger number of new therapies, but also better therapies by allowing individual entrepreneurs to take on more innovative but riskier projects rather than playing it safe, and then spreading these risks over a larger pool of investors. Quantity and quality can both be improved through better financing tools and business models.

Finance need not be a zero-sum game. And at least in this one instance, we can all do well by doing good.

Thank you for your time and attention to these important issues, and I would be happy to answer any questions from the committee.

Conflicts of Interest Statement

Andrew Lo reports personal investments in private biotech companies, biotech venture capital funds, and mutual funds. Lo is a co-founder and partner of QLS Advisors, a healthcare analytics company; an advisor to BrightEdge Ventures and Thales; an advisor to and investor in BridgeBio Pharma; a director of Roivant Sciences Ltd., the MIT Whitehead Institute for Biomedical Research, and Annual Reviews; chairman emeritus and senior advisor to AlphaSimplex Group; and a member of the Board of Overseers at Beth Israel Deaconess Medical Center and the NIH's National Center for Advancing Translational Sciences Advisory Council (pending confirmation) and Cures Acceleration Network Review Board (pending confirmation).

During the most recent six-year period, Lo has received speaking/consulting fees, honoraria, or other forms of compensation from: AIG, AlphaSimplex Group, BIS, Boston Consulting Group, BridgeBio Pharma, Citigroup, Chicago Mercantile Exchange, Financial Times, Harvard University, IMF, National Bank of Belgium, Q Group, Roivant Sciences, Scotia Bank, State Street Bank, University of Chicago, and Yale University.

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