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CASE STUDIES

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BUSINESS MODELS TO CURE RARE DISEASE: A CASE STUDY OF SOLID BIOSCIENCES

Esther S. Kim[a,b] *and Andrew W. Lo*[a,c,d,e,*]

Duchenne muscular dystrophy (DMD) is a rare genetic disorder affecting thousands of individuals, mainly young males, worldwide. Currently, the disease has no cure, and is fatal in all cases. Advances in our understanding of the disease and innovations in basic science have recently allowed biotechnology companies to pursue promising treatment candidates for the disease, but so far, only one drug with limited application has achieved FDA approval. In this case study, we profile the work of an early-stage life sciences company, Solid Biosciences, founded by a father of a young boy with DMD. In particular, we discuss Solid's one-disease focus and its strategy to treat the disease with a diversified portfolio of approaches. The company is currently building a product pipeline consisting of genetic interventions, small molecules and biologics, and assistive devices, each aimed at addressing a different aspect of DMD. We highlight the potential for Solid's business model and portfolio to achieve breakthrough treatments for the DMD patient community.

[a]MIT Laboratory for Financial Engineering, Sloan School of Management, Cambridge, MA
[b]MIT Technology and Policy Program, Cambridge, MA
[c]MIT Computer Science and Artificial Intelligence Laboratory, Cambridge, MA
[d]MIT Department of Electrical Engineering and Computer Science, Cambridge, MA
[e]AlphaSimplex Group LLC, Cambridge, MA
*Corresponding author. E-mail: alo-admin@mit.edu

1 Introduction

Drug development is a risky and costly endeavor, requiring more than 10 years and $2.5 billion for a single successful candidate to reach the market (DiMasi, 2014). The process is capital-intensive, each milestone on a drug candidate's timeline requiring millions of dollars for such

items as discovery, animal model studies, clinical trials, regulatory filings, and marketing and sales. As a result, biopharma companies have generally focused on developing assets for lucrative and usually large markets (Pammolli *et al.*, 2011). In recent years, however, policy incentives and strong opportunities for commercialization have driven biopharma companies to increase research and development for rare and orphan diseases (Meekings *et al.*, 2012), which affect smaller populations, but present significant unmet medical needs.

Historically, orphan and rare diseases, defined by the FDA as diseases with fewer than two hundred thousand cases in the U.S., have largely been neglected, since drug developers have had little incentive to develop treatments for few patients. Currently, 7,000 of these rare diseases affect a total of 30 million individuals in the U.S. (FDA, 2016a). In 1983, congressional legislation created the FDA's Orphan Drug Designation, which gives incentives to orphan drug developers to develop treatments for rare diseases. Since then, the number of approved orphan and rare drug treatments has grown significantly, with more than 550 products on the market since the passage of the legislation (FDA, 2016c). Despite this progress, developers of drugs for rare diseases (now including big pharma and biotechnology companies) still face significant scientific and financial risks, and many rare diseases still present significant unmet needs. Among the diseases still without a proven and effective U.S.-approved treatment is Duchenne muscular dystrophy (DMD), a fatal and rare genetic disease with an incidence of approximately 1 in 5,000 males, primarily among young boys, worldwide (Hoffman and Connor, 2013).

In recent years, the FDA has announced the possibility of accelerated approval for DMD drug candidates. This is an attempt to create incentives and stimulate development of therapies for the DMD patient population. The extended DMD community has been waiting for a treatment for decades (FDA, 2014). Recently, there has been an increase in momentum in DMD drug development, with a handful of companies actively developing treatments for DMD patients. The persistent involvement and advocacy of the DMD patient community underscores the urgent need for a successful treatment.

This need is still unmet. In the past year, the FDA has rejected initially promising drug candidates from PTC and BioMarin, candidates that had been championed by the DMD patient community. In a recent victory for the community, however, Sarepta, another company working on DMD drug development, has gained accelerated approval from the FDA for its drug, eteplirsen, which targets approximately 13% of DMD patients. Nevertheless, the company must continue to run studies to show the safety and efficacy of the drug, and the approval may be subject to withdrawal based on further findings.

In this case study, we discuss the work of one life sciences company, DMD-focused Solid Biosciences, founded by the parents of a young boy with DMD. This young company has achieved several promising early successes. We highlight its unique business model and its potential to achieve further breakthroughs in developing long-awaited DMD treatments. Specifically, we emphasize Solid Biosciences' one-disease focus and modality-agnostic approach to developing drug candidates for DMD. We analyze the potential of this model to mitigate the challenges associated with drug development and successfully bring to market treatments for patients with rare diseases.

2 Background

Rare and orphan diseases are defined by the FDA as those that affect fewer than 200,000 individuals

in the United States. Starting in 1983, congressional legislation has created policy mechanisms to accelerate innovation and development for rare diseases with target populations too small to financially justify large research and development programs. Through this legislation, the Orphan Drug Designation was created, which provides seven years of market exclusivity for the first developer to achieve approval for a candidate. Since the legislation was enacted, more than 550 orphan drugs have been approved (FDA, 2016c), compared to just 10 from 1973 to 1983 (FDA, 2016b). Companies that have developed these drugs have done quite well during the exclusivity period (Meekings *et al.*, 2012), offering an attractive investment for investors and the biopharma companies that develop the drugs. While some of the candidates that fall under this category are novel, others are part of partially developed asset programs that had been previously shut down, or are candidates initially developed for other indications.

Despite the success of the Orphan Drug Designation, there are still many untapped opportunities in drug development, particularly for rare and orphan diseases. Declining research and development activity in the pharmaceutical industry has resulted in many promising early-stage candidates that fail to advance to the clinic for further study, let alone to patients. Because of the significant cost and time required for drug development, investors are more likely to fund later-stage assets that have achieved proof of concept, or those assets that have the potential to become blockbuster drugs. Meanwhile, mergers and acquisitions in the pharmaceutical industry have become increasingly common, and large biopharma and biotech companies often acquire the early work of smaller biotech companies that do the early development and "de-risking" of assets. With pharmaceutical companies losing significant value due to stagnant R&D productivity (Garnier, 2008) and investors averse to early-stage assets, there is a significant lost opportunity in the development of potential therapies for patients. However, recent trends show that the pharmaceutical industry is experiencing economically favorable returns with orphan drugs (Meekings *et al.*, 2012) and, as a result, unaddressed rare and orphan indications offer a potentially lucrative area for future drug development.

2.1 Duchenne muscular dystrophy

Duchenne muscular dystrophy is a severely debilitating muscle disease caused by a genetic mutation on the X chromosome, resulting in the lack of dystrophin, a protein that is critical for establishing muscle stability (Fairclough, 2013). Currently, there is only one approved treatment for a small subset of DMD patients and no cure in the United States for this rare disease, which disproportionately affects young boys (and in rare cases, girls). The current standard of care involves palliative options and the use of steroids, which result in significant side effects in children. Despite its classification, DMD is one of the more prevalent "rare" diseases in the U.S., and places a significant disease burden on families, communities, and the healthcare system. The disease is fatal in all boys, most requiring wheelchairs by age 12 and dying due to heart failure or respiratory difficulties in their twenties (Fairclough, 2013). It is estimated that approximately 10,000–15,000 boys suffer from DMD in the U.S., translating to a national economic burden of nearly $500–800 million annually (Larkindale *et al.*, 2014).

3 Company history

Solid Biosciences is a private life sciences company based in the Kendall Square biotech hub in Cambridge, Massachusetts. The company was founded by Ilan Ganot, Gilad Hayeem and Andrey Zarur soon after Ganot's son was diagnosed with

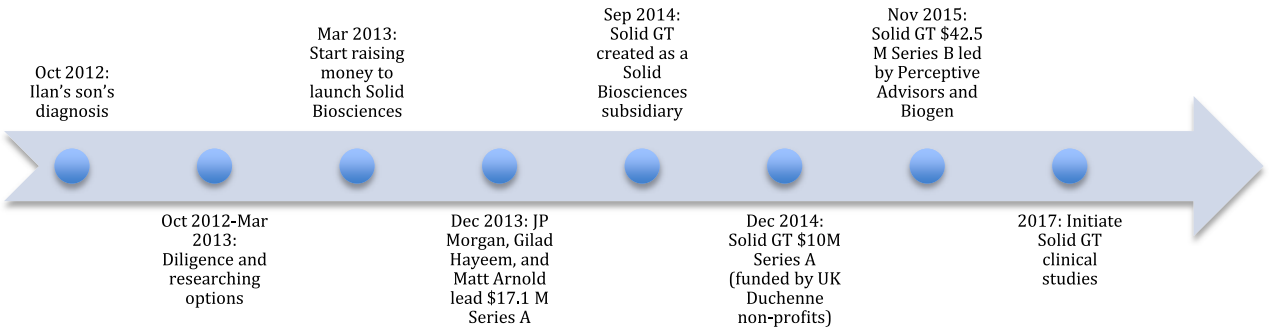

Figure 1 Key company milestones.

DMD in 2012. The company's name, Solid, is the English translation of his son's Hebrew name, Eytani.

As a parent, Ganot was frustrated with the lack of progress in DMD drug development, but as Solid's future CEO, he also saw a commercial opportunity for a new company that would address this unmet medical need. Prior to founding Solid, Ganot had been an investment banker with JPMorgan Chase, and had years of experience in corporate finance and structuring deals. The early Solid team considered a range of options for making a contribution to DMD research and development, from creating a nonprofit organization to establishing an investment firm, before ultimately deciding that a hands-on drug development company would maximize its impact on the DMD population. With that, Solid's current business model was born.

Soon after founding Solid, Ganot discovered that many pharmaceutical companies and academic institutions had promising early-stage investigational candidates for DMD that had stalled in development. Ganot and his first hire, Joel Schneider, a former graduate student in DMD research, now a director of Solid's research and development program, reviewed the landscape of DMD assets for potential breakthrough applications, including gene therapy. The company ultimately decided to in-license intellectual property for a gene therapy candidate for DMD. Soon after, Ganot convened a conference with many of the major DMD researchers working on gene therapy in the U.S., leading to some of Solid's first academic partnerships.

Since its founding in 2013, Solid has established itself as a center of excellence for DMD research and drug development. It currently operates four platforms: Assistive Devices, currently developing the Solid Suit, a DMD assistive device; Disease Modifying Therapies, for biologic and small molecule assets that address the multiple secondary disorders that result from DMD; Disease Understanding, which strives to use biomarkers to improve diagnoses and the understanding of the impact of therapy; and Corrective Therapies, which includes its gene therapy platform under the company's subsidiary, Solid GT.

4 Company funding and operations

Based on its proposed business plan and its articulation of an unmet need in DMD, Solid Biosciences was able to raise $17 million in its Series A fundraising in 2013. A critical early backer of Solid was JPMorgan, Ganot's employer at the time he learned of Eytani's diagnosis. JPMorgan invested $5 million into the Series A round for Solid, and it currently holds a seat on Solid's board of directors. In addition, Gilad Hayeem, one of the company's cofounders, and current board member Matthew Arnold, each invested

in the round. The two are currently the biggest individual shareholders of the company.

The backing of JPMorgan was critical in Solid's early stages. It was an uncharacteristic step for the financial services firm, which does not typically participate in one-off venture investing, let alone in an employee venture. However, JPMorgan was preparing for the IPO of a biotech company also working on DMD, and thus understood the business opportunity and its unmet medical need. Furthermore, Ganot's story had percolated within the company and received internal support, including from JPMorgan's CEO, Jamie Dimon. The investment did not fall neatly inside JPMorgan's existing lines—not in the bank's charitable investing unit, its impact investing department, or its private investments. Nevertheless, the firm's senior executives believed investing in the cause was the right thing to do, and rallied behind Ganot and his family. Over the course of nine months, the details were ironed out and due diligence was completed, allowing JPMorgan to lead the first financing round.

One key early decision at Solid was to dive deep into gene therapy for DMD. Solid GT, a Solid Biosciences subsidiary, was formed, and in December 2014, a Series A round was completed. This complemented Solid Bioscience's $5 million of investment with an additional $5 million of capital, which was invested in return for equity ownership of Solid GT by three prominent U.K.-based DMD charities: DMD Research Fund, DMD Children's Trust, and Joining Jack. This partnership with DMD-focused organizations was instrumental in providing a promising start for Solid GT. Each organization, in addition to its capital, was able to provide expertise, leadership, and a keen sense of urgency.

In November 2015, Solid GT closed a $42.5 million Series B round, led by the investment fund Perceptive Advisors, which focuses on healthcare, and by the biotechnology company Biogen, to continue development of its Corrective Therapies platform. Unlike Solid Biosciences' first round of fundraising, the management team was able to raise money for Solid GT based on the progress of its scientific work, specifically, the promising preclinical data for its lead gene therapy candidate, SGT-001. Executives from Biogen and Perceptive Advisors have since joined the Solid GT Board of Directors.

4.1 Company management

Solid Biosciences is an operating company, now with more than 25 employees, which oversees four platforms, Disease Modifying Therapies, Assistive Devices, Disease Understanding, and Corrective Therapies, the last of which is held within Solid GT, a formal subsidiary of the Company. The platforms encompass Solid's work in small molecules and biologics, assistive devices, biomarkers, and genetic interventions, respectively. The company operates under its CEO and management team, with active and regular participation by its board members. Ganot, the CEO, runs the day-to-day operations of the company. Gilad Hayeem, currently a Solid board member and its president, also runs the investment management firm Waverly Capital, based in New York City. Andrey Zarur currently serves as the chairman of the Solid Biosciences board. Business decisions and activities are initiated by the management team, and are reviewed by the management boards. Currently, there is a dedicated Board of Directors and Scientific Advisory Board for Solid's subsidiary, Solid GT, in addition to

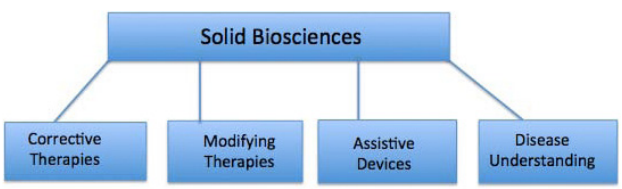

Figure 2 Company structure.

the Board of Directors for the umbrella company, Solid Biosciences.

5 The Solid portfolio

Solid's complete focus on understanding DMD gives it a unique edge when considering potential asset acquisitions and licenses. The management team naturally looks at groundbreaking science, commercial potential, and the likelihood of clinical success. However, the most important factor for Solid is that the science must have the potential to be translated into a therapy for DMD patients. A central tenet of Solid's strategy is that if Solid focuses on the science with the most potential in DMD, financial reward will follow. In addition, because Solid is modality- and technology-agnostic, it is not tied down to any particular class of asset or scientific approach. This method has allowed the company to make quick shutdown decisions when data was unpromising or not indicative of future clinical success.

In general, when evaluating potential assets, Solid leverages its scientific expertise in DMD to pursue peer-reviewed research initiated and conducted by leading DMD researchers in the field. In addition to its business analysis of an asset (including the potential target market), the Solid team favors assets that have shown promise in animal models, or better still, that have promising human data. Because animal models are not perfectly indicative of an asset's performance in humans, poor data from animal studies is not necessarily a deal breaker, if the scientific advisory and management team feels that there is potential efficacy for DMD patients.

Solid is able to make holistic decisions about assets. Key to this process is the expertise of the advisors, clinicians, and experts on Solid's advisory board, who help to reduce risk when the management team is considering potential assets and making important decisions. Solid's focus on a single disease has attracted a strong community of scientific and clinical experts, which provides Solid with a key strategic advantage in developing its portfolio of candidates.

Solid's strength is its ability to focus its asset review on DMD alone. Because it knows the space and competitive landscape so well, Solid is able to avoid redundancy. While the company still actively researches and pursues potential in-licensing opportunities, Solid is now on the receiving end of licensing offers from other researchers and companies who are familiar with its work and focus on DMD.

Solid outsources research and development, helping to manage offsite labs, largely at academic research centers. Solid not only funds these labs, but also strategizes and thinks through scientific decisions with them, bringing its DMD expertise to the table. In alignment with its strategy of being modality-agnostic, Solid has a portfolio ranging from genetic intervention and secondary disorder management to Solid Suit, an exoskeleton device for children with DMD to wear. As of 2016, Solid's assets are all in the preclinical stage, and represent a diverse range of potential solutions for DMD patients.

5.1 Corrective therapies and Solid GT

Through its Corrective Therapies platform, Solid is pursuing therapeutic approaches that address the underlying cause of the disease to benefit as many DMD patients as possible. The company's biggest bet in this effort is the application of gene therapy to replace the defective gene responsible for DMD. Gene therapy was first shown to work in patients with melanoma in 1990 (Collins and Thrasher, 2015), but it still has not been approved in the U.S.

In 2016, the European Medicines Agency (EMA) approved its second gene therapy, used for the treatment of a rare metabolic disorder, ADA-SCID, for the European market (Mullard, 2016). While gene therapy is still in its infancy, with challenges ranging from gene delivery in patients to manufacturing and production, Solid Biosciences sees recent advances in methods in the biotechnology industry as bringing about the "third wave" of gene therapy efforts.

Solid Bioscience's subsidiary, Solid GT, has made progress in Corrective Therapies for DMD. Thus far, it has been involved in successful preclinical animal studies of its lead gene therapy candidate, SGT-001. The data from these studies has helped Solid GT raise approximately $50 million for additional development, and the company plans to initiate clinical trials for SGT-001 in 2017. Significant challenges still remain for gene therapy. Challenges specific to DMD gene therapy include the systematic delivery of the gene to all affected muscles, as well as significant hurdles in manufacturing and immunological response to the therapy. Furthermore, there is the challenge that gene therapy, if successful for DMD patients, would only prevent further damage, but will not be able to address muscle degeneration that has already occurred.

5.2 Disease modifying therapies

In addition to its Corrective Therapies platform, Solid is building a pipeline of small molecule and biologic assets, which have the potential to address the secondary disorders that result from DMD (see Figure 3). Most of the assets, which must show utility in DMD, are or will be in-licensed from other organizations, or developed in partnership with other organizations. For example, in 2016 Solid established a collaboration with Strykagen to investigate Galectin-1, a preclinical biologic candidate that has the potential to improve muscle regeneration and repair through multiple biologic pathways.

5.3 Assistive devices

Solid Biosciences' assistive device platform focuses on devices that may help patients perform everyday activities with greater ease. The platform currently encompasses the company's

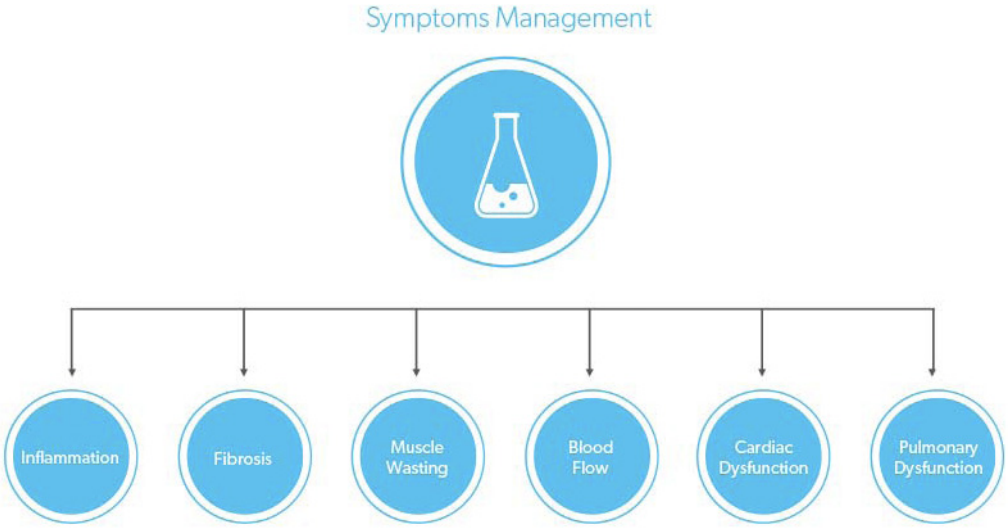

Figure 3 Solid's Disease Modifying Therapy approach.

activities in developing an exoskeleton suit for children with DMD, called the Solid Suit. Solid added the suit to its portfolio after recognizing that patients were physically limited in ways that could be alleviated through an innovation like the Solid Suit. Unlike the other candidates in its portfolio, which address the biochemical causes of DMD, the Solid Suit addresses a previously unmet need discovered through its close interactions with the patient community. In fact, Parent Project Muscular Dystrophy, a leading U.S.-based patient advocacy group, founded by a mother of two sons with DMD, is one of the noteworthy partners in the development of the Solid Suit, providing unparalleled information, connections, and access to patients and opinions that continue to influence the development effort.

5.4 Disease understanding

Solid's Disease Understanding platform focuses on research and development to identify new potential biomarkers for measuring the progression of DMD. At present, many existing DMD clinical trials use expensive and invasive muscle biopsies to measure the dystrophin protein levels in affected patients. Alternatively, studies may employ gross motor function tests. However, these assessments do not necessarily provide biochemical information about the impact of a DMD therapy on the human body. Solid is looking to supplement current tests by examining potential DMD biomarkers in serum or urine to identify additional relevant clinical endpoints. While there is a growing amount research to identify DMD biomarkers (Hathout *et al.*, 2016), no effective serum and urine biomarkers have been validated for DMD clinical trials. The company hopes that its work will lead to an improved understanding of DMD's disease progression and provide synergistic opportunities for enhanced clinical trials with their existing pipeline.

6 Analysis of business model

Solid Biosciences identifies itself as a disease-focused company that pursues multiple approaches with the potential to benefit DMD patients. As a "one-condition" company, Solid balances its singular focus with diversification in its research and development strategy. Its focus on a single disease gives the company a competitive advantage, and establishes it as a center of excellence for DMD, allowing it to gain significant business and scientific expertise in therapeutic development. Equally, Solid achieves strategic diversification in two ways: by targeting various points along the pathological cascade experienced by DMD patients, and by pursuing varied approaches to the treatment of DMD. It is able to achieve portfolio diversification by targeting distinct yet complementary approaches, while simultaneously pursuing methods to better understand and measure the underlying biology of the disease. In addition, a diversified approach is consistent with Solid's modality-agnostic strategy, not tying itself to any particular cure or technology platform.

A common model in the biopharmaceutical industry is to apply a compound or modality to as many different indications as possible. Solid takes the opposite approach, and applies as many viable modalities as possible to one disease. Solid's strategy, in essence, is to take many well-selected "shots on goal," all of which are complementary, and where one success does not take away from the possibility of success in other areas. While the DMD-causing gene mutation, and its subsequent pathology, have been well characterized, the reasons for the mutation are still unknown. While some mutations are hereditary, a significant portion occurs spontaneously (Fairclough, 2013). Because of the heterogeneity in its disease biology, DMD, like many diseases, manifests and expresses itself in different ways in

different patients. Furthermore, the mutation and the accompanying lack of the dystrophin protein result in numerous associated disorders that offer several targets for further research and development. As a result, Solid's assets may be useful to address the various phenotypes and associated challenges of DMD patients.

Beyond the strategic approach of its portfolio, Solid's one-disease model allows it to be efficient, nimble, and focused. Because it can convene the top scientific experts, key patient groups, and top talent, Solid is able to leverage this expertise to mitigate the many scientific and financial challenges associated with drug development.

6.1 Keys to success

Like other biotech companies with responsibilities to its investors, Solid Biosciences defines success through its valuation, which is driven by scientific progress and reaching its milestones. As the parent of a son with DMD, Ilan Ganot is a strong parental advocate within the DMD community. His direct ties and personal understanding of the medical and human experiences of DMD patients enable the company to identify and tackle significant problems in the treatment of DMD. At the same time, as the CEO of a company focused on DMD, Ganot and his team must manage potential conflicts of interest. Solid has implemented measures to ensure its objectivity by creating a governance system to check and review management decisions. As a result of mitigating this risk, Ganot's personal ties and motivation serve as assets when meeting with existing and potential investors, rather than potential conflicts.

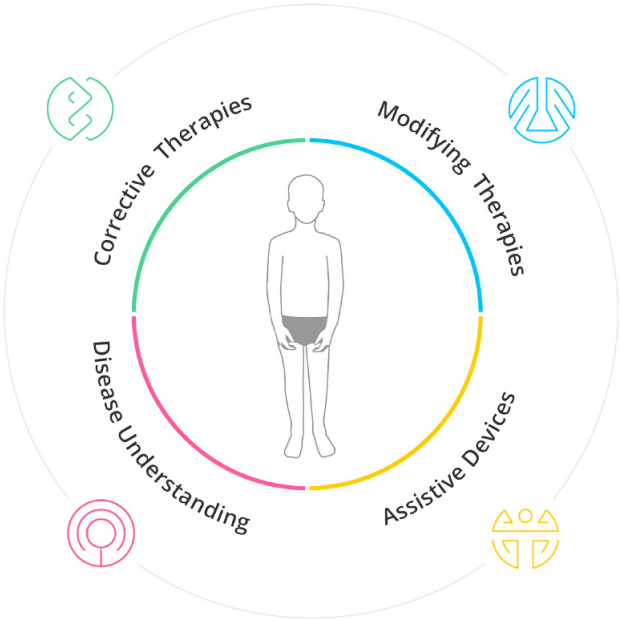

Figure 4 Complementary approaches under a one-condition focus.

Furthermore, the company has been able to assemble an impressive board and advisory committee of DMD experts, who not only provide credibility for its work, but also advise its management decisions. Solid has been successful in convening experts and encouraging collaborative work between them. Having the top DMD experts on its board to advise Solid provides a significant advantage over biotech companies that may apply a technology platform more diffusely across several diseases.

Finally, an undeniable key to Solid's success is Ganot's single-minded determination to find a treatment for DMD, not only for his son, but also for all patients with DMD. Under Ganot's leadership, Solid is solely and genuinely focused on improving the lives of patients with DMD. This single-minded determination is reflected in the mission of the company, as well as its business strategy. Solid is successful because it focuses on the problem first, and then looks for the best solutions and approaches to solve it. To help operationalize this effort, Solid's team consists of people who believe in its mission to treat DMD patients with the best therapies as quickly as possible, and are committed to developing a treatment for the DMD community. Before Solid's

Series B fundraising, a number of pharmaceutical giants offered to partner with Solid and potentially buy it, based on the company's promising SGT-001 gene therapy results. Solid turned down the offers in order to maintain its control of the development of its gene therapy platform. Selling an asset and leaving its future in the hands of another company does not align with Solid's mission. Ganot had already observed that larger pharmaceutical companies often choose not to pursue development of early-stage assets, whether due to risk, limited resources, or more attractive options in their vast portfolios.

6.2 Patient perspective

An instrumental key to Solid's success is its support from DMD patients, families, and advocacy groups, which together comprise an extremely close-knit community. This support is not merely financial. For years, this community has joined forces to advocate for more research and progress in DMD drug development; and for years, it faced a series of disappointing updates, or worse, a lack of interest in this rare disease. Today, however, the drug development landscape is quite different, with many companies seeking to develop therapies for rare diseases, motivated not only by an unmet medical need, but also the promise of a significant return on investment.

For Solid Biosciences, the involvement of DMD patients and their parents is critical. Keeping the patient's perspective in mind during development allows Solid to understand the true pain points of patients and the clinical effects of the current standard of care. Many of Solid's employees maintain close ties with the patient community. The company's employees regularly attend DMD patient conferences, and Annie Ganot, Eytani's mother, heads Solid's patient advocacy efforts, helping the company establish strong relationships with the DMD community globally. Furthermore, leaders of major DMD patient organizations have backed Solid by funding and advising its research and development activities. Examples include Parent Project Muscular Dystrophy, which invested in the Solid Suit and has collaborated with the company on other activities; DMD Research Fund; DMD Children's Trust; Joining Jack, which co-founded Solid GT; and a number of additional partnerships with DMD groups worldwide. Solid's one-condition focus has been instrumental in developing these partnerships with DMD patient organizations, which recognize Solid's dedication and commitment to the same disease.

7 Challenges and future plans

Since 2013, Solid has achieved significant milestones and built a pipeline of promising assets with the potential to treat DMD patients. However, drug development is a risky and costly endeavor for any company, and Solid Biosciences is no exception. Moreover, Ganot is a first-time CEO and a newcomer to drug development. As it stands, Solid relies heavily on partnerships with third-party companies, labs, and manufacturers for its work. In addition, like many biotech companies, Solid will need to rely on partners for its manufacturing and distribution capabilities. Because Solid's mission is to reach the global DMD patient population, partnerships are considered the primary means to achieve this goal.

One criticism of the company is: with so many approaches, is Solid really able to focus its activities to achieve success? Solid, like other early biotech companies, has limited resources, and it must decide how to allocate funds across its portfolio. If it pursues too many assets and approaches, it risks limiting success in any given approach. From Solid's perspective as a drug developer and patient advocate, however, it identifies the work that it finds most promising for DMD patients and attempts to bring it closer to market. As it grows and progresses, Solid will

have to address increasing development costs as its assets enter the clinical stage. Furthermore, because of Ganot's personal ties to the disease, Solid will need to continue to maintain its objectivity in its business decisions to select and shut down assets that no longer hold sufficient promise.

In order for Solid to bring a therapy to patients, it will also need to overcome the challenges of clinical development in human studies, which require significant time, personnel, creativity, and funds. So far, none of its candidates have yet entered the clinical stage, which will be a large milestone for the company. These studies cost millions of dollars, and Solid will need to raise the funds to design, initiate, and complete them. In particular, gene therapy, Solid's biggest undertaking, will incur significant costs and resources in clinical trials.

Solid is also working to nurture further therapeutic innovation by training the next generation of leading researchers and scientists in DMD. It has established the Solid Fellows program, which trains postdoctoral researchers at universities currently active in DMD research, and it is setting up partnerships with universities to lay a foundation for continued and future DMD research. Part of Solid's vision is to invest in academic research that could potentially lead to next-generation therapeutics for DMD patients. So far, the company has invested money in more than 15 academic research labs to continue and support DMD research.

8 Conclusion

The stakes for DMD drug development are extremely high. Hundreds of boys and young men die every year from this rare disease, yet drug development for it has been riddled with failure. Several companies have filed DMD candidate drugs for approval with the FDA, but only one has achieved this goal. News of a rejected candidate is a setback for the entire DMD community of patients and families, including Ganot and his family. While Solid does not have a candidate in clinical trials, the team has been vigilantly watching these developments. These recent FDA decisions have provided Solid Biosciences with important knowledge about the approval process, and have helped the company better understand the agency's position on matters such as dystrophin expression, the need for sufficient endpoints, and the high threshold for FDA approval.

In this case study, we have highlighted Solid Biosciences' business model. Solid Biosciences' one-disease focus on DMD has enabled it to achieve significant milestones relatively quickly and efficiently, and have made it a center of excellence for research, attracting patient groups, researchers, advisors, and investors to join its mission. Solid's expertise in DMD enables it to diversify its projects and approaches strategically. Still, Solid faces several hurdles ahead as it enters the clinical stage, where any candidate's chances of success are low (DiMasi, 2014).

As interest in developing therapies for rare and orphan diseases increases in the biopharma industry, it is fruitful to consider business models that could result in faster cures with lowered risk. A diversified, one-condition approach has the potential to be a model for other biotech companies to emulate in rare disease drug development. Furthermore, investors may find this model of development to be more attractive than traditional models in which a single technology platform is applied to multiple and varied indications.

Beyond creative business models, however, drug development for rare diseases like DMD could be helped by external systemic changes that incentivize or accelerate development. While beyond the scope of this discussion, policy changes are a

critical area for further inquiry to speed up innovation for rare diseases. The Orphan Drug Designation has already been successful in attracting drug developers to study long-neglected diseases. Additional policies that accelerate the approval process, or modify the thresholds for approval, may be able to help bring drugs to the millions of U.S. patients with rare diseases but limited or no treatment options.

For decades, the DMD patient advocacy community has been waiting and pushing for treatments for DMD. Every month or year that a treatment is delayed, thousands of children further deteriorate. Ilan Ganot's son, Eytani, is now six years old, and is increasingly showing symptoms of DMD. However, there is hope in the patient community that a cure or an effective treatment is achievable. More than ever, the scientific community's understanding of DMD and its biology is of increasing use in drug development. Technological and scientific advances have allowed companies like Solid Biosciences, which employ strategic business models to minimize their risk while maximizing their chance of success, to take innovative approaches to drug development, toward the ultimate goal of achieving the long-desired breakthrough treatments for the DMD patient community.

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Author contributions

Both authors contributed equally. A.W.L. first conceived the idea of writing a case study of Solid Biosciences and held several meetings with I. Ganot in preparation for the study. Interviews were arranged and conducted by E.K. in consultation with A.W.L. Both authors contributed to the preparation of the manuscript.

Competing interests

E.S.K. declares that she has no competing interests. A.W.L. reports personal investments in BridgeBio Capital (also an advisor), ImmuneXcite, KEW, MPM Capital, Novalere, Royalty Pharma, and Visionscope, and is a director of the MIT Whitehead Institute and Roivant Sciences.

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Bios of Interviewees

Ilan Ganot, CEO and Co-Founder of Solid Biosciences. Mr. Ganot is Founder and Chief Executive Officer of Solid Biosciences and Solid GT, and a member of the board of directors of both companies. He started Solid in 2013 to find treatments, and potentially a cure, for Duchenne muscular dystrophy, a disease that afflicts his son Eytani. Prior to starting Solid, Mr. Ganot was an investment banker at JPMorgan Chase in London, specializing in hedge fund-driven equities business for the firm. Mr. Ganot also worked at Nomura Securities in London, Hong Kong, and New York, where he managed relationships with investors and clients of the firm. Prior to Nomura, Mr. Ganot was a senior salesperson for Lehman Brothers' European Equities business. Mr. Ganot embarked on a banking career after practicing law at the Israeli law firm, Haim Zadok & Co, where his focus was private equity law and mergers and acquisitions. Prior to practicing law, Mr. Ganot was division head at Vir-Tech, a laser engraving business, and a captain in the Israel Defense Forces. Mr. Ganot received his MBA from London Business School and holds law and business degrees from the IDC in Herzliya, Israel.

Gilad Hayeem, Co-Founder of Solid Biosciences and Managing Partner at Waverly Capital. Gilad Hayeem is a member of the board of directors of Solid Biosciences and Solid GT and is an active manager. Mr. Hayeem founded Solid Biosciences through his family office, Waverly Capital, and led the Series A round alongside JPMorgan. Mr. Hayeem was Managing Partner and CEO of Marble Bar Asset Management, a UK based investment fund he founded in 2002, which he exited in 2010. Mr. Hayeem then moved to New York, where he lives with his wife and four children. Mr. Hayeem received his MBA from City University, London, and holds history and politics degrees from the University of Leeds, England.

Andrey Zarur, Co-Founder and Chairman of the Board of Solid Biosciences. Andrey Zarur

is Founder and Chairman of the Board of Solid. Dr. Zarur has been active in early-stage life sciences companies for more than 20 years, and has participated in the creation of more than a dozen companies in the healthcare and clean energy sectors. He is also Chairman, CEO, and Founder of GreenLight Biosciences, and a partner at Kodiak Venture Partners, a venture capital firm specializing in the formation of early-stage information and life technology investments. Prior to joining Kodiak Venture Partners, he was founder and CEO of BioProcessors, which was sold to Seahorse Biosciences in 2007. In addition to BioProcessors, he has led four life science companies from inception to exit. Dr. Zarur is also a cofounder and chairman of the board for Lumicell, and chairman of the board for Allegro Diagnostics. Dr. Zarur was named a Young Global Leader of the World Economic Forum in 2005. He is an Overseer of the Museum of Science in Boston and a Senior Lecturer at the Massachusetts Institute of Technology (MIT) Sloan School of Management. Dr. Zarur holds Masters of Science degrees and a Ph.D. in Chemical Engineering from MIT and undergraduate degrees from the National University of Mexico. Dr. Zarur is the author of several peer-reviewed articles and holds close to 100 provisional and issued patents.

Carl Morris, VP of Research and Development of Solid Biosciences. Carl Morris is the Vice-President of Research and Development, responsible for overseeing the drug development processes for Solid Biosciences. Prior to joining Solid, Dr. Morris was a Senior Director for Pfizer's Rare Disease Research Unit, leading their efforts in neurologic diseases and the muscle biology programs. While at Pfizer, Dr. Morris directed several small molecule, and biotherapeutic development programs, including a program that led to a Phase 2 study in Duchenne Muscular Dystrophy, while also heading an internal research group responsible for advancing programs from target identification to the clinic for many of the rare neurologic and muscle-related diseases. Dr. Morris identified key external opportunities, and worked closely with patient groups, academic laboratories, and other industry partners to advance drug development in the rare neuromuscular space. His scientific and drug development experience at Pfizer also included investigations into broader muscle wasting conditions, as well as tendon and bone repair biology. Prior to joining Pfizer in 2007, Dr. Morris was an Assistant Professor at Boston University School of Medicine, and a founding faculty member of the Muscle and Aging Research Unit, established to investigate strategies for improving muscle function during aging or disease. He completed his Postdoctoral fellowship in the Department of Physiology at the University of Pennsylvania, where he worked on multiple projects, ranging from molecular aspects of muscle protein interactions to therapeutic approaches for modulating muscle size and function. As a trained muscle physiologist, his academic pursuits have ranged from biophysical aspects of muscle contraction and enzyme kinetics to therapeutic interventions in a variety of *in vivo* muscle atrophy and disease models. Dr. Morris holds a B.A. in Biology from Franklin Pierce College (Rindge, NH) and a Ph.D. in Physiology from UCLA.

Joel Schneider, Director of Research and Development. Joel Schneider is the Director of Research & Development for Solid, responsible for the identification and development of promising therapies for DMD. Dr. Schneider's R&D focus includes Solid's gene therapy, small molecule, and biologics programs. Dr. Schneider previously completed a postdoctoral fellowship at Harvard University in the Department of Stem Cell and Regenerative Biology, characterizing and developing small molecules that enhance skeletal muscle regeneration. He holds a Ph.D.

from Rutgers University and an undergraduate degree from Brandeis University. During his doctoral work, Dr. Schneider studied the cardiomyopathy associated with Duchenne muscular dystrophy and is the author of numerous peer-reviewed articles related to Duchenne muscular dystrophy and stem cell biology.

Andrea Ponti, Executive Partner and Founder, GHO Capital. Andrea Ponti has 30 years of investment banking experience, focusing on healthcare since 1996. He created both JP Morgan's and Goldman Sachs' European investment banking healthcare franchises, advising on transactions for leading pharmaceutical, medical device and hospital companies. Over the last five years, he was Vice Chairman of European Investment Banking and Global co-head of Healthcare at J.P. Morgan. Prior to that, Andrea was at Goldman Sachs, where he was Partner, Managing Director, Head of European Healthcare, Consumer and Retail and also Co-Global Head of Healthcare. Andrea sits on the board of Cell Medica, and received a B.A. in Economics from the University of North Carolina at Chapel Hill, where he is also a member of the Arts and Sciences Foundation Board of Directors.

Pat Furlong, CEO of Parent Project Muscular Dystrophy. Pat Furlong is the Founding President and CEO of Parent Project Muscular Dystrophy (PPMD), the largest nonprofit organization in the United States solely focused on DMD muscular dystrophy. Its mission is to improve the treatment, quality of life, and long-term outlook for all individuals affected by DMD through research, advocacy, education, and compassion. Along with leading PPMD, Pat speaks about DMD and related topics at conferences each year worldwide, and is an active Board member with the Genetic Alliance and the Muscular Dystrophy Coordinating Committee, U.S. Department of Health & Human Services. Pat graduated from Mt. St. Joseph College with a B.S. in Nursing, and also attended graduate school at Ohio State University.