

WHITE PAPER

# SEIZING OPPORTUNITIES IN THE CURRENT LIFE SCIENCES ENVIRONMENT: VENTURE APPROACHES

## Seeing the opportunities and seizing them with leadership, strategy, and execution

In continuing our work from the HBS Kraft Accelerator, we regularly hold meetings with leaders from across the private sector, disease foundations, academia, and government to focus on trends, strategies, successes, and best practices in accelerating the development of cures.

We recently hosted a meeting focused on:

- The current life sciences funding environment
- Venture philanthropy success stories that focused on leadership, strategy, and execution

### Key Takeaways

- Even in a much more challenging life sciences funding environment, venture philanthropy opportunities exist.
- For those disease foundations interested in venture philanthropy, what matters most is leadership, a clear strategy, and creative, effective execution.

## CURRENT LIFE SCIENCES FUNDING ENVIRONMENT

HBS alums Arjun Goyal, MD, MPhil, MBA and Stefan Vitorovic, MS, MBA, both co-founders and managing directors at Vida Ventures, a leading life sciences venture capital firm, shared what they are seeing in the current funding environment. Arjun Goyal summarized the current situation by stating, “It’s the best of times, it’s the worst of times.”

### Best of Times

Reasons given for a positive outlook about life sciences include:

- Over the last few years, there has been a huge fervor for the life sciences industry and enthusiasm for biotechnology, which was further fueled by the pandemic.
- A great deal of capital, including capital from “generalist” investors, flowed into the industry.
- A large amount of private capital has been raised by life sciences funds over the last few years and continues to be raised from investors with longer-term views, including pension funds, endowments, and family offices.



**“YOU SHOULD HAVE CONFIDENCE THAT IF YOUR SCIENCE IS GOOD AND ACTIONABLE, IT CAN BE TRANSLATED INTO IMPACTFUL MEDICINES FOR PATIENTS IN NEED OF NEW THERAPEUTIC OPTIONS. THEN, THERE’S STILL ENOUGH CAPITAL—ACTUALLY A LOT OF CAPITAL AROUND—FOR THOSE EFFORTS.”**

ARJUN GOYAL

- Over the past two years, around \$50 billion in private capital has been raised, and investment funds have raised \$5 to 10 billion for dedicated life sciences investments in just the past few months.
- A great deal of this capital remains in dry powder, with investors sitting on lots of cash.
- Deals are still happening and many companies that have raised capital continue to make progress and show positive results.
- Large pharma is in a very strong position and is sitting on a great deal of cash. Pharma’s biggest problem right now is loss of exclusivity due to patent expiration. To fill these voids, pharma is willing to spend. “When they want to buy something, they go and buy it,” said Stefan Vitorovic. Pharma is looking at phase 3, de-risked assets and is very happy to pay 2X or 3X what they paid a year or two ago. However, with increased FTC scrutiny of large deals, pharma is also doing a great deal of earlier-stage business development partnerships and equity investments.

### Worst of Times

At the time that funds continue to raise and sit on large amounts of capital, “The fundraising environment has changed dramatically,” said an industry expert.

- In the last few years, there has been a tripling or a quadrupling of the number of biotech companies. Due to the low cost of capital, numerous companies were funded that should not have been started, because their science was not yet ready.
- Also, hundreds of life sciences companies went public earlier in their life than has been typical, without first significantly de-risking.

- Now, a significant “culling of the herd” will be taking place as many companies are struggling to raise capital and to survive.
- The capital markets for biotech and life sciences have been troubled since early 2021.
- Indices are down from 40% to 50% during this time and are down even more—in the 60% to 80% range—for smaller companies, with the results varying based on the therapeutic area.
- The ROIC has diminished.
- Those experiencing the worst returns have been the new, inexperienced investors—“the tourists”—who are now exiting the life sciences/biotech market.
- Some public companies are currently trading below the value of their cash. Some will fail but there are good companies with real assets that are undervalued. Some investors are creating “opportunity funds” to take advantage of these opportunities.

**“I THINK HEALTH AND DRUG EXPENDITURES ARE GOING TO BE UNDER PRESSURE . . . WE’RE IN A TOUGH ENVIRONMENT FOR A WHILE.”**

PARTICIPANT

### Other Factors Affecting the Current Environment

Beyond just positive and negative sentiments, meeting participants expressed additional sentiments about the current funding landscape.

- We’ve been here before.** There have been other boom and bust cycles in biotech and life sciences, even in the past few decades. When this happens, the tourists get out of the biotech business.
- Opportunities exist for focused experts.** For investors who understand the science, have connections, have a long-term view, and are flush with cash, there will be tremendous opportunities.
- There is significant regulatory uncertainty.** The Biden Administration appears to be of multiple minds about healthcare, pharma, and biotech. And, it appears the FDA is going to be very restrictive and risk averse for a while, as evidenced by the decision about Biogen’s Alzheimer’s drug.

- **There is significant uncertainty about academia’s focus on science.** Even before endowments have been hit, universities have pulled back their support for science. While universities still have plenty of money, their level of support for science is uncertain.

- **Philanthropy is likely to be reduced.** People who had a lot of money prior the recent stock market volatility still have a lot of money, but they are likely to be more cautious about their philanthropic commitments.

One foundation CEO explained that high net worth individuals who have created family foundations must distribute 5% of their foundation’s assets each year. Distributions for 2022 were calculated based on the value of the foundation’s assets at the end of 2021, which was a good year for the stock market. As a result, “There is a ton of philanthropic capital that needs to be distributed this year,” said one foundation CEO. However, based on the current state of the markets, assets held in family foundations may decline in 2022, making 2023 a potentially difficult year for philanthropy.

- **Partnering with nonprofit disease-focused funds will remain of interest.** Stefan Vitorovic said there are multiple benefits to working with nonprofit disease-focused organizations. These benefits include access to patients and biospecimens, more efficient trial recruitment, access to opinion leaders, better understanding of patients, and an increased ability to engage with regulatory bodies about patient-driven outcomes. For these reasons, investors are often interested in including and working with disease-focused entities, especially in a more capital-constrained environment. However, for both an investor and a disease-focused organization, there must be a good strategic fit.

#### Key Takeaways about current funding environment

- The life sciences funding environment is now more difficult than in has been.
- However, even in this more difficult environment, opportunities still exist for great science and great leadership teams.

“WHAT [PARTNERING WITH NONPROFIT, DISEASE-FOCUSED FUNDS] MEANS IS A HIGHER PROBABILITY OF SUCCESS, HIGHER PROBABILITY OF NOT ONLY REACHING THE GOALPOSTS BUT ALSO GETTING SOMETHING THAT PATIENTS ACTUALLY CARE ABOUT. THIS TRANSLATES TO HIGHER COMMERCIAL SUCCESS, POTENTIALLY BETTER DESIGNED TRIALS, AND FASTER TIMELINES. ALL OF THESE THINGS IN A MORE CAPITAL CONSTRAINED ENVIRONMENT BECOME ACUTELY IMPORTANT.

STEFAN VITOROVIC



## HOW THE EB RESEARCH PARTNERSHIP (EBRP) IS VENTURING INTO CURES

Epidermolysis Bullosa (EB) is a family of rare genetic disorders that affect the skin. EB Research Partnership, founded in 2010, is driven by the mission to cure EB by 2030 and to lead the way for rare diseases.

### Background on Rare Diseases

There are about 7,000 rare diseases, 80% of which are caused by a faulty gene. Currently, 95% of rare diseases lack an FDA-approved treatment. Half of rare diseases do not have a foundation or a research support group.

### EBRP History & Impact

Since 2011, EBRP has raised \$45 million, funded 105 research projects, and formed four companies. EBRP has funded work involved with 19 out of 39 active clinical trials focused on EB. All of EBRP’s projects have been under venture philanthropy agreements.

“100% OF EBRP’S RESEARCH PROJECTS HAVE BEEN FUNDED UNDER VENTURE AGREEMENTS. I THINK THAT MAKES US UNIQUE IN THAT WE DON’T PUT A PENNY OUT THE DOOR UNLESS WE HAVE A VENTURE PHILANTHROPY AGREEMENT. ALMOST EVERY ONE HAS SOME SORT OF AN EQUITY STAKE.”

MICHAEL HUND

### EBRP Funding Model Evolution

As shown below, EBRP’s funding model has evolved.



Initially, EBRP funded academic medical centers under venture philanthropy models. Then, the organization started funding private and public companies through the same scientific advisory board application process. Based on receiving applications for funding from startups, EBRP concluded it could take the lead in forming companies, putting management teams in place, and taking equity stakes. Finally, after having funded projects and formed companies, EBRP decided to create an investment fund.

EBRP’s CEO shared four venture philanthropy case studies that showed EBRP’s experience as an investor seeking to fund cures for this rare disease.

#### CASE STUDY 1: REALIZING A 6X ROI FROM TRADITIONAL VENTURE PHILANTHROPY

EBRP provided \$500,000 in funding under a venture philanthropy agreement to a university to develop a treatment for severe EB that corrects gene mutations in skin cells. A public biotech company used the IP that was developed to make a treatment; EBRP received stock in that biotech. EBRP sold its shares in the company for \$3 million, realizing a 6X return on its investment. Those funds were directed back into future research projects.

“Most importantly, we helped advance research into the hands of a public pharmaceutical company to make a treatment, which would not have occurred if we hadn’t been an angel investor early on and invested in the university,” said Michael Hund.

#### CASE STUDY 2: MAKING A 2X RETURN AND ELEVATING A PROMISING THERAPY

EBRP awarded a \$770,000 grant under the organization’s venture philanthropy model to Krystal Biotech, a public company that was developing a topical gene therapy for EB. In less than six months EBRP was able to sell its shares in Krystal for more than double the original investment, generating an ROI of over 110% and reinvesting that capital back into more EB projects.

Most importantly, EBRP helped elevate the company to a phase 2 clinical trial. At that point, Krystal had no problem raising additional capital. The company has reported positive data and recently filed for FDA approval.

“WE DOUBLED OUR INVESTMENT AND HELPED ELEVATE THAT TREATMENT TO A POINT WHERE NOW IT’S KNOCKING ON THE DOOR TO BE THE FIRST EVER APPROVED TREATMENT FOR EB AND ONE OF THE FIRST EVER TOPICAL GENE THERAPIES.”

MICHAEL HUND

#### CASE STUDY 3: SPINNING OUT TECHNOLOGY TO FORM A NEW COMPANY

EBRP awarded \$5 million to ProQR, a Netherlands-based public company, for development of an exon skipping technology. ProQR ended up coming back to EBRP with news that it was going to deprioritize this work to focus on other company priorities.

EBRP decided to spin out ProQR’s exon skipping technology, bring in a management team, and form a completely new company—Wings Therapeutics—to take this technology forward. EBRP became a significant equity holder in Wings.

#### CASE STUDY 4: FORMING A FOR-PROFIT HOLDING COMPANY

After EBRP had founded four companies, the organization decided to put three of these assets into a for-profit holding company, Phoenicis. To maximize the value of its portfolio and of this holding company, EBRP asked, “How can we expand the pie and make this appealing to investors?”

The answer was to look to apply the technology and IP that was developed beyond just skin diseases and beyond just rare diseases. Based on an insight that skin diseases are inherently inflammatory diseases, Phoenicis decided to focus on first-in-class treatments for rare, genetic, and inflammatory diseases with multiple “shots on goal” for orphan, breakthrough, and pediatric designations.

This holding company has partnered with other disease organizations to bring other assets into the holding company. The holding company is looking to raise capital and to leverage its assets more broadly than just EB.

## Lessons Learned

Based on these experiences, EBRP has learned three important lessons.

1. **Grow the funding pie.** EBRP is able to raise far more investor capital than philanthropic capital as a rare disease foundation. At that same time, EBRP was able to raise more philanthropic capital because donors like the organization’s direction and its initiatives.

“THE BIGGEST THING FOR ME AS A CEO IS THAT THIS HAS COMPLETELY CHANGED THE CONVERSATIONS WE HAVE WITH HIGH NET WORTH INDIVIDUALS. I SAY, ‘WHAT NEED DO YOU HAVE FOR YOUR CAPITAL? ARE YOU SEEKING RETURNS FROM HIGH-RISK, HIGH-REWARD INVESTMENTS? DO YOU NEED A PHILANTHROPIC TAX WRITE-OFF? IT’S A BRAND NEW CONVERSATION.’”

MICHAEL HUND

2. **Have a patient-first, value-creation mentality.** The holding company, founded by patient organizations, has enshrined a patient-first mentality. This mentality is paired with a data platform, which increases the ability to quickly recruit clinical trials and enables real-time dialogue with patient communities. Collectively, this creates synergy and provides scale.

3. **Want economics and control—but not too much control.** EBRP doesn’t want any semblance of control in investments. EBRP doesn’t want board seats or voting rights, and wants to keep its equity at less than 20% of a company.

### Key Takeaways about EBRP’s experience

- Creative, nimble leadership and effective execution—even when difficult—matter greatly.
- EBRP, under Michael Hund, has continued to learn, evolve, and adapt to achieve greater scale and to pursue new opportunities to develop treatments for patients.



## THE ALPHA-1 FOUNDATION’S TAP

Alpha-1 antitrypsin deficiency (Alpha-1) is a genetically inherited condition that may result in serious lung or liver disease. It’s believe that there are at least 100,000 people in the US who have this condition, and most don’t know it, making detection and diagnosis critical.

In the mid-2010s, the Alpha-1 Foundation (A1F) created The Alpha-1 Program (“TAP”) to support new drug discovery and development by investing in pharmaceutical companies with highly promising compounds and devices.

In November 2019, the A1F board voted to suspend future investments by TAP due to transitional challenges related to leadership changes. TAP as a legal entity still existed and existing contracts were still honored.

Then, in October 2021, Scott Santarella was hired as president and CEO and in June 2022, a former investment banker became chair of the board. With these leadership changes, both the CEO and the chair of the board are strongly “pro venture philanthropy.” They are looking to reinvigorate the TAP program and are in the process of evaluating potential investment opportunities as well as reinstating existing opportunities.

**“WE GOT STALLED BECAUSE OF TRANSITIONAL CHALLENGES IN LEADERSHIP. IT’S MY GOAL TO BRING IT BACK TO FRUITION.”**

SCOTT SANTARELLA

As of mid-2022, the value of the assets in the TAP program was about \$28 million, with about \$11 million in cash. To date, TAP has committed about \$4 million in 12 investments. Among TAP’s current investments are:

- Arrowhead Pharmaceuticals, RNA interference (Phase 2)
- Mereo BioPharma, oral anti-protease (Phase 2)
- Dicerna, RNA interference (Phase 2)
- pH Pharma, oral anti-protease (Phase 2)
- Inhibrx, recombinant AAT (Phase 1)
- APICBIC, gene therapy (pre-clinical)

In addition, AIF has created a therapeutic development network that includes about 50 clinical research centers and is launching a pilot project with the sole focus of driving clinical trials and recruitment for trials. AIF also has a 2,800-person patient registry, a bio consortium of about 500 annotated samples, and a sister organization that handles about 8,000 patients who receive augmentation therapy on a monthly basis.

From a fundraising perspective, AIF has had tremendous support from companies that provide augmentation therapy, who provide support for a wide variety of programs and services, with programs modeled after MMRF.

#### **Key Takeaways about AIF’s experience**

- Leadership and strategy matter. Without supportive leadership, TAP raised about \$30 million and made investments in 12 promising companies. The, without strong and supportive leadership, AIF’s involvement in venture philanthropy languished.
- Now with a new CEO and a new Board Chair who are pro-venture—who have made venture philanthropy a strategic priority—AIF is once again primed to seize opportunities and take advantage of venture philanthropy as a catalyst for accelerating development of treatments.