All responses from participants are included below, alphabetized by First Name.

1. What is one of your favorite science papers you have read in the past year? What excites you about this work, or the area more broadly?

David Baker put out a paper on computational design of passively permeable macrocyclic peptides that I found interesting (<u>link</u>). Macrocycles are a bit of a "tweener" between small molecules and large biomolecules. In certain cases, you can get macrocycles that engage a target akin to a biologic but are also sufficiently small molecule-like to enable oral delivery (e.g., MK-0616). Peptide chemists can only churn through so much chemical space, so accelerating that process with a computational approach could be super interesting, and might practically help drug developers generate more of these types of therapies down the road. **- Alex Loftis, Vida**

We are constantly learning more about the how the ever-present conflict between humans and viruses – mobile genetic elements, both external and even in our own genome, have shaped our biology. Recently in Nature (https://www.nature.com/articles/s41586-024-07095-8), we learned how this conflict helped us lose our tails. There are still many mobile elements yet to be characterized that we've co-opted for essential biological processes that, one day, may be used to inform therapeutics or even serve as therapeutic tools themselves. - Alim Ladha, MPM

I really loved this paper describing the screening of an ultra-large virtual library of novel agonists for the serotonergic 5-HT_{2A}R receptor. The screening efforts led to the discovery of potent agonists with unusual downstream GPCR signaling kinetics, and when tested in mice, had antidepressant-like effects on behavior without exhibiting hallucinogenic-like properties. Neuropsych is a hard place for drug discovery, but I thought this was a remarkable effort combining computational and empirical structural biology, medicinal chemistry, and animal behavior toward the rational design of novel ligands for a validated CNS target. - Aniqa Tasnim, 5AM Ventures

Over a decade ago, the concept of tumor drug addiction was introduced (<u>Das Thakur et al.</u>, <u>Nature 2013</u>), proposing a new translational oncology paradigm whereby BRAF-treated tumors become both resistant but also paradoxically dependent on BRAF inhibition, which was later shown to be mechanistically driven by <u>activation of ERK</u> signaling in response to BRAF inhibitors. Fast forward to last year, work out of the Sellers Lab (<u>Chang et al.</u>, <u>Nature 2023</u>) has broadly contextualized the concept of oncogenic activation lethality, showcasing that in certain tumors, just like in Melanoma / BRAF, there are pathway dependencies which are based on genetic activation rather than inhibition. The biotech industry has classically thought of drugs as inhibiting proteins, yet this work reveals there's a highly differentiated way to think about

attacking tumors, and importantly doing so in a truly smarter way that out-smarts the cancer (rather than just hitting something harder!).

Building upon elegant work out of the Sanger Institute a couple of years ago, <u>Wang and colleagues</u> elegantly showcased translational utility for the emerging concept of somatic mosaicism – clonal remodeling of cells via postzygotic mutations – as a driver of pathology in NAFLD. The researchers introduced somatic mutations into mouse livers and proceeded to study the clonal competition and downstream fitness effects these clones conferred, observing that a protective phenotype was attributed in certain scenarios of increased genetic somatic mutation carrying clones. We've classically thought of somatic mutations as genetic drivers in cancer but have yet to thoroughly look at the opportunity outside of oncology, and thus this work suggests there is a new opportunity ahead for elucidating the genetic predisposition of noncancer diseases (I&I, metabolic, neurodegenerative), potentially offering a new frontier of genetic-led precision medicine. - Artie Arumov, Qiming

<u>Li et al., 2023</u> is a notable example of the intersection of next-generation biology with cuttingedge chemistry. My background is in computational biology, but the fundamental basis of drug discovery is chemistry by nature, so the transition to venture has help me appreciate this spectrum. Examples like this highlight instances where both fields contribute to accessing the non-druggable space to positively impact patients. **- Danjuma Quarless, Abbvie Ventures**

The great thing about biotech is that markets may suffer but there is no recession in science. Here's one of many papers I enjoyed: "Whole-body cellular mapping in mouse using standard IgG antibodies." The authors improve upon previous clearing processes to render the mouse optically transparent. There's a lot of fascinating visualizations of various structures the authors show, particularly the lymphatic system. I would recommend checking out the supplementary videos of the paper when you get the chance. As Ethan Garner had taught me back at Harvard, there is something just wonderful about being able to directly observe things. - David Yang, Lux Capital

An exciting paper I read this year was a preprint from Klebl, McMillan *et al.*, Swinging lever mechanism of myosin directly demonstrated by time-resolved cryoEM. While I am sure we've all seen the rendered GIFs of myosin "walking" along actin filaments, this paper captured for the first time the myosin "primed state" just before the power stroke which had only ever been hypothesized to exist. This is such a perfect example of what excites me about science, a group of innovators visualizing something that we never did before, unlocking foundational knowledge piece by piece that we hope ultimately allows new medicines to be developed. **- Harry Won, OUP**

Revisiting the dogma of antibody drug conjugates – Raffaele Colombo from Zymeworks. This was a great paper and presentation at AACR last year which challenges some of the tightly held traditional beliefs about ADCs. The authors do a great job of examining how the first generation of ADCs haven't necessarily delivered on their promise of widening the therapeutic index of their

associated toxin and examine some of the paradoxes around next-gen stable linkers. Given the explosion in the number of pre-clinical ADC companies the paper is great food for thought as we think about how novel payloads, linkers, conjugation sites and targets could translate in to more efficacious and safer drugs. - James Buxton, NEA

It is hard to understate the impact of incretin-based therapies on medicine. The associated clinical trial literature published in just the last few years is rich; see Kosiborod et al., N Eng J Med 2023 as an example. In medical school – close to a decade ago for me – we were taught the already-important role of GLP-1 in diabetes care. Few of us foresaw the eventual use cases across a broader range of conditions. - Kevin Li, Frazier Life Sciences

The <u>Dou et al. 2024</u> paper looking at the role of Xist in autoimmunity was an incredibly cool publication. Historically, academia does such a poor job of incorporating sex-specific differences between male and female mice, because frankly it just makes it harder to run experiments. But we know in humans across a plethora of diseases from Alzheimer's to SLE that sex plays a significant, understudied role in disease susceptibility, pathogenesis, and progression. I've been mulling over the implications of this paper for therapeutic development and haven't found any clearly druggable targets yet, but hope this encourages more groups to do this type of research in the future. **- Lauren Mifflin, Frazier Life Sciences**

Taking some liberties with the question here – the first episode of one of my favorite podcasts this year, "Acquired" covered Novo Nordisk and Ozempic. Despite not being a healthcare-focused podcast, I appreciated their thoughtful and bite-sized approach to navigating the complex healthcare backdrop in which Novo Nordisk became what it did today, including the early rivalry between Novo and Nordisk that fueled some of the groundbreaking research in diabetes. It's also a great primer to share with people who don't have a scientific or healthcare background – which I appreciate! - Nil Gural, Polaris

I think it's exciting that we will improve overall drug discovery by incorporating AI technology, this includes the reduction of time from hit to lead optimization and DC nomination. As a result, we will have more defined biomarker approaches in Oncology, Immunology and other related diseases to accelerate clinical trials and identify the most appropriate pt populations that will respond early to any given therapy. I think the most relevant is the recent publication in Nature Biotechnology that describes just this: a novel SM targeting TNIK in fibrosis, which was tested in Ph1 trials among healthy volunteers, i.e. Insilico Medicine. We also have a portfolio company, Scorpion Therapeutics that is doing the same in Oncology. Also, I am drawn to work in obesity and neuropsychiatry. The innovation that we have made in these two spaces and will continue to make within the next 5 years is going to be astonishing! We are no longer working in scientific discipline silos, and learning how scientific discovery is interconnected: for example, obesity drugs will also impact inflammatory conditions. Nature: https://www.nature.com/articles/d41586-024-00118-4 - Noelle Hutchins, Omega Funds

One of the papers that took me down many rabbit holes in the past year was "Emergent autonomous scientific research capabilities of large language models" by Boiko et al, which was also recently published in Nature. Currently, lab automation enables scientists to regain time that can be redirected toward higher risk/reward experiments that do not require industrialization (exploration), in addition to enhancing the reliability and replicability of workflows that are repeated often (exploitation). This paper, FutureHouse's mission statement and several other papers like this one, highlight how an Al copilot can enhance scientists' productivity even further by shortening the experimental cycle. It aids in the design of experiments, accelerates execution of experiments and semi-autonomously analyzes results to propose improvements for the subsequent cycle. Another key point in the paper is that LLMs have an impact in biosecurity through the democratization of previously hard-to-access knowledge. Anthropic, OpenAl and National Security Commission on Emerging Biotechnology are all investigating the potential risks for LLMs as a biosecurity threat. While this intersection may not currently represent the bulk of today's biosecurity risk, it is an increasingly important consideration - Pablo Lubroth, Hummingbird

I like outliers. So I get excited when I read something that is very different from anything I've seen in the past. Even better if it's a bit under the radar and confusing. That sweet spot between confusion and understanding can reveal entirely new worlds. A recent example is this preprint from Andrew Fire's group where they discover RNA "Obelisks". These obelisks are circular RNAs ~1kb in size, predicted to form rod-like secondary structures, and even have ORFs coding for a novel protein superfamily they term "Oblins". Really weird stuff. From a biotech perspective a few things come to mind of potential interest: (1) the mechanism of circularization for such a large circRNA molecule (could it compete with other RNA circularization methods?), (2) the stability of the molecule, and (3) translation efficiency. The science here is obviously very early (too early for a company), but nonetheless gives an example of the types of science I like to track. - Patrick Lundgren, Hummingbird

One of my favorite papers of 2023 was Jones et al's NEJM publication, "Selective Inhibition of NaV1.8 with VX-548 for Acute Pain." The authors report two PhII studies demonstrating that VX-548, a non-opioid, oral, small molecule inhibitor of NaV1.8 developed by Vertex, provides significant acute pain relief following abdominoplasty or bunionectomy. There's a tremendous societal need for non-opioid alternatives for acute and chronic pain relief, and Vertex has done a great job laying the groundwork for NaV1.8 inhibitors to be considered a promising and emerging therapeutic class in these settings. **- Roman Camarda, Novo Holdings US**

One of the most impactful science papers I came across in 2023 was published in the NEJM and titled "Base-Edited CAR7 T Cells for Relapsed T-Cell Acute Lymphoblastic Leukemia." It's the first paper, to my knowledge, that showcases the application of base-edited CAR-T cells for treating stubborn leukemia. This article resonated deeply with me because I have witnessed the devastating toll T-ALL takes on children and their families. Knowing that T-ALL can affect children as young as 2 years old makes the urgency of such breakthroughs even more apparent. Reading about this treatment left me pondering what could have been if it had existed a decade ago to potentially save the life of someone I love. I'm excited about the broader



implications of base editing in addressing various disorders. I believe this technology holds immense promise and will pave the way for numerous new treatments in the years ahead. - Sahil Chopra, Vertex Ventures HC

A recent 2024 paper I found interesting related to assessment of proteomic techniques for early cancer detection, using a high plex (3072) assay. The level of performance was impressive, showing early detection utility in 18 solid tumors (though the sample size is relatively limited/retrospective). Notably, low concentration biomarkers were particularly high utility, and the most specific proteins for cancer detection were actually ones that were downregulated rather than upregulated. Overall this is promising for the future of early detention, a space that sorely needs higher sensitivity, cost effective solutions. https://bmioncology.bmj.com/content/3/1/e000073 - Shoman Kasbekar, Foresite

This is not quite related to my day job, but I found this <u>scientific paper</u> from last year quite interesting. It reports the first documented case of 'virgin birth' in crocodiles, a type of reproduction known as 'facultative parthenogenesis,' which also occurs in other species, including snakes, birds, and lizards. Fascinating! - Suan Tuang, TCGX

"Glioblastoma remodeling of human neural circuits decreases survival" Nature 2023 https://www.nature.com/articles/s41586-023-06036-1. This is beautiful work at the intersection of neuroscience and tumor biology. Here, Michelle Monje and Shawn Hervey-Jumper explore the role of functional connectivity between glioma cells and neurons and how these connections influence cognition and drive disease progression. They go on to show that disrupting communication between neurons and glioma cells inhibits proliferative and migratory potential of GBM, leading to improved survival. One of my take-aways is a call to broaden our aperture to include non-cell-autonomous aspects of tumor biology to think about ways of deliberately identifying and targeting tumor-parenchymal interactions in high-grade gliomas and beyond. - Travis Hughes, Digitalis

2. How did you get involved in venture? What drew you in? What initial misconceptions did you have about biotech venture investing or creation?

After defending my PhD, I dipped my toe into VC through the Vida fellowship in Boston. I really enjoyed my time there and felt I learned a lot about the industry in the process. After that I went off to work on strategy and buy-side DD projects as a life sciences consultant, worked on a spin out based on my graduate research, and found myself contemplating exits from consulting where I'd be able to do a similar mix of things. By complete coincidence, I found out from Mark Springel (on Vida's Boston team) that Vida's LA team was looking for someone to work on due diligence and early-stage builds, which sounded like a perfect fit. This led me to my current role and back to my hometown of LA! - Alex Loftis, Vida

I've always found investing to be an exciting career path – it's analytical, involves constantly learning, and, over the long run, is extremely meritocratic. At some point, research got a hold of me and took me on a different path, and, through that, I was exposed to the wonderful world of biotech and startups. The fact that venture marries these two areas quite perfectly drew me in for a long-term career. - Alim Ladha, MPM

My journey to venture began in college when I enrolled in a biomedical engineering intro course at University of Rochester. With a curriculum focused on experiential learning and projects that frequently interfaced with the medical center, I was immediately intrigued by the potential to have transformative impact in healthcare. A standout memory was from a final project in Biosystems & Circuits, in which we designed and built a communication platform for patients with Locked-in Syndrome, a rare disorder that causes total body paralysis except for eye movement. With this excitement, I did a speedrun toward any opportunity that would support my pursuit of a career as a tenured professor, which was (at the time) my end-all be-all. While working on my PhD thesis at MIT, located in the heart of the Kendall Square life science innovation cluster. I started to understand the diversity of opportunities within biotech/biopharma that stretch beyond academia. I tried on different hats, including in venture creation (Flagship Pioneering), healthcare investing (RA Capital), biopharma (Novartis), and boutique consulting (Clarion), After graduating, I joined Satellite Bio, a start-up spun out of my thesis lab. As one of the first employees, I focused primarily on operational excellence for our R&D and TechOps teams, but felt disconnected from strategic discussions that helped set the broader company timelines and milestones. I leveraged my network for warm intros to new potential roles to help fill this knowledge gap. I ultimately became most excited about a venture capital fund called Vertex Ventures HC (VVHC), and was fortunate to join the investment team in September 2022.

- Amanda Chen, Vertex Ventures HC

I was planning for academia for the long haul for as long as I can remember, and I was really lucky to have an incredible PhD advisor and lab. In my fourth year, I remember distinctly talking to my lab mate Mark Springel (now at Vida Ventures), distraught about how I was going to choose a postdoc lab when the universe of science was so wide - I knew I was most excited about science not at my own bench, but at talks, conferences, and engaging with projects across areas. Ultimately my conversations with Mark and several others who were also very generous with their time led me to fellowships with the Harvard Office of Technology Development (OTD), Civilization Ventures, and Vida Ventures. I was totally immersed in earlystage, impactful science through these experiences and had incredible mentors throughout. While I was at OTD, Deb Palestrant (5AM, 4:59 Initiative) spoke at OTD's Bench to Business bootcamp about her experiences as a biotech company builder, operator, and investor. This got me very excited about 5AM /4:59's venture creation and investment model (and anyone that has met Deb knows she is totally magnetic), and I was incredibly fortunate to join the team in 2023. On venture creation - 5AM's scientific rigor and institutional expertise in operationalizing earlystage innovations through the 4:59 Initiative (including but not limited to pieces like HR and putting together the right team, legal/IP, real estate, accounting, pipeline prioritization, and forming the right syndicate), have completely shifted how I think about all of the elements -



beyond the fundamental science – needed for an early-stage venture to maximize likelihood of success. - Aniqa Tasnim, 5AM Ventures

Before entering the VC world, I had thought that the best science always wins and that if you were developing a new therapy based on a strong translational hypothesis and data package, you'd be given the chance to push the project forward into the clinic and improve upon unmet need. I eventually began realizing that this was certainly not the case, and that there are a range of additional factors that are needed for the success of new therapeutic development, many stretching beyond the technicalities of the data. Building an organization that's aligned and acting in unison on a day-to-day level, with a story that resonates across various key stakeholders (e.g., encompassing competition, sensible milestones and workplans), each with their own different sticking points, is paramount to success. I was drawn to venture to learn more about the considerations that are needed alongside the strong translational science, and started off with a full-time fellowship (big shoutout to the amazing Will McConnell for taking the initial call!!) that allowed me to be fully immersed in all day-to-day activities for 2.5 months. Fellowships are a great way to experience what a true life in VC looks like and gauging if it's what you thought it would've been, if you like it enough to stay in it, or not. - Artie Arumov, Qiming

After starting my career as a research scientist, my contributions over time earned me opportunities to join leadership and governance sessions at AbbVie. These were my first experiences with our BD and strategy groups, which led me to join a 2-year development program. AbbVie Ventures was one of the four rotations I completed, and I found the work incredibly engaging and exciting- it didn't feel like work. What drew me in were 1) the ability to engage the entrepreneurial ecosystem at large, which is vibrant and exciting, and 2) the opportunity to review and have exposure to many scientific disciplines and technologies. An early misconception I had was that venture investing and company creation were solely about science and research. However, I quickly learned that relationships and the quality of a leadership team are broadly considered most important. - Danjuma Quarless, AbbVie Ventures

I had my start in venture capital with Lux Capital. One of the many aspects that drew me to VC was the ability to understand the full gamut of business models for biotech commercialization. I had been working on a prototype software for biotechs to collaborate better with CROs, but found myself stuck often around GTM strategy and process. During these times, conversations with VC friends were often most clarifying and ultimately led to me taking an interest in joining one. This led me to Lux Capital where I invested and incubated life sciences companies, and I'm continuing this work at Lux Capital. During my early days, I was surprised to learn what considered a "good outcome" in venture, especially for a large fund. I had thought even \$100mm would be an exciting exit size, but for a \$400mm fund with a 20% ownership in this company this returns just 5% of the fund. Such outcomes can be great for the founder of course, but it's why large funds often focus on the large home-run outcomes. The fund size is your strategy. **- David Yang, Lux Capital**

During the pandemic and my third year of grad school, I had a lot of time to be self-reflective and realized that I wanted to be much closer to seeing innovations become medicines that help patients. There is a wide universe of these roles, so I got involved with the Harvard Biotech Club and Nucleate to learn more. I explored different options, mainly by speaking to people in those careers. At this stage, I didn't really have misconceptions, rather more that I had no idea what VC was at all. Learning that I would get to see the most cutting-edge science being built into new therapeutics was enough to get me interested. To learn more, I applied to VC fellowships and joined Vida Ventures as a Fellow. I found that much of the job entailed the aspects of science I loved the most (e.g., critically analyzing biological data – diligence; thinking through experimental design and strategy - portfolio company support) across many disciplines. modalities, and therapeutic areas. In fact, I often describe biotech VC as being a lot like journal club, except instead of a paper, it's focused on actual startup's data. I was curious about venture creation, and so joined Flagship Pioneering as a Fellow and had the opportunity to experience our industry from a totally different lens. Both experiences highlighted that biotech VC was where I could find the match of my skillsets, innate curiosity, drive to contribute to therapeutic development, and insatiable desire to be constantly working on different things. I had the opportunity to join OUP last April and was thrilled to jump in! - Harry Won, OUP

I've always been interested in basic and translational science and ventures is one of the few jobs that gives you almost continuous exposure to cutting edge science while also affording you the chance to work in many different capacities. I started getting involved during business school and was lucky enough to work at a few places before joining NEA. Initially I thought the work would be more individual and siloed but I'm fortunate enough to work with great colleagues everyday. - James Buxton, NEA

When I was in my second year of medical school, the treatment paradigm for hepatitis C completely changed. It suddenly went from a largely incurable disease to a highly treatable infection with a 96% cure rate after only three months of taking a benign pill. I explored how the standard of care changed so quickly and discovered the entrepreneurs, scientists, and investors who helped make that change possible, including researchers at the University of Alabama. What surprised me was that transformative innovations can happen outside of the universities with the highest research dollars. According to the National Science Foundation database the University of Alabama ranks 143 in research spending in recent years. Innovation can be found in many places, and it's important to maintain academic relationships to come across these interesting opportunities. - Jason Wang, Frazier Life Sciences

I worked in basic and translational science research throughout undergrad, explored health outcomes research in medical school, and served biotech, pharma, and healthcare provider clients while in consulting. Across these experiences, I discovered biotech investing as a perfect intersection of biology, chemistry, (patho)physiology, business, and patient care, all of which I found intellectually stimulating and personally fulfilling. My first experience with my current firm was through a summer internship during medical school, which materialized from a cold email. I

had a great experience and was excited to have the opportunity to come back following medical residency. **- Kevin Li, Frazier Life Sciences**

I started my career as a management consultant. After one particularly frustrating client meeting, a coworker said to me "you know, I think you'd like private equity or venture capital because you own/control the company and can actually set the strategy rather than having to listen to your clients". In retrospect, that comment isn't entirely too accurate, but when I had the opportunity to do my MBA at Chicago Booth, I spent most of my time either taking immunology classes or pursuing VC-centric coursework and internships. I was lucky to spend nearly two years doing health tech investing 3 days per week at Jump Capital during my MBA, where I learned that VC is an incredibly cool job, but that I'm not great with tech and missed early-stage science. So when I subsequently did my PhD, I was fortunate to find a similar opportunity as a Fellow with the 5AM Ventures team where everything fell into place and I found that I love biotech company building and early stage investing in the life sciences. My biggest misconception was that venture is venture is venture – every firm does biotech investing and creation differently, and like PhD labs, there's no one perfect firm for everyone, but I believe there is a perfect firm for each individual. - Lauren Mifflin, Frazier Life Sciences

I worked at a biotech company before grad school and loved my experience. I knew I wanted to dedicate my career to developing novel therapies to treat patients with devastating disease. This motivated me to go to grad school. I stayed in academia after grad school because I loved new discoveries but I was also frustrated by how slow things moved from the bench to bedside. I wanted to be actively developing therapies that stem from new ideas, so I decided to venture into biotech creation. TRV enables me to do precisely that – take an early idea, often from academic collaborators, and help build the science, strategy and business to advance the idea to an actual medicine. It's complex and challenging but fun and very rewarding. - Linda Vo, TRV

The long and short of it is that I wanted to work on cool translational science that could be impactful for patients and to learn from great people how drugs are made.

Having seen during my MD/PhD training a drug target I worked on go into clinical trials and fail, I was curious to learn the why & how drug discovery programs and technologies succeed or not in translating into medicines. Atlas biotech venture creation & early-stage investment model felt like a great environment to do just that. I am exposed every day to new science, I get to analyze the journey of different biotechs, and spend my days working side-by-side with veteran drug hunters getting new companies off the ground. The above was not always obvious of course. Towards the end of my PhD biotech VC jobs felt attractive but also nebulous and opaque, and I was worried that transitioning into the industry meant I would stop being a scientist. Being a Fellow at Vida Venture (Investing) and Flagship Pioneering (Company building) dispelled that misconception and showed me I really enjoyed the job. Experiencing the two firms/models also made apparent that Atlas was the ideal model & culture fit for me. - Maurizio Fazio, Atlas

I was fortunate to do my PhD in a lab that exposed me to venture early on. My advisor spun out a number of companies, graduate students in the lab followed careers in venture and

entrepreneurship and all that left me with a sense that a career in venture could be thrilling. I went on to management consulting after finishing up in lab and fast forward a few years, right around the time I was itching to get back closer to science, my advisor connected me to Polaris. While what got me interested originally was the proximity to innovation, what drew me in was the people. I get to work in a firm where culture and collaboration is paramount and unlike most of the industry, where women are in leadership positions. What I didn't appreciate enough coming into the job is the role we as investors can play in helping a company grow. In that sense, investing, at least the way we do it, is less about having a crystal ball into the future and more about establishing a relationship with the founders, supporting them in good and bad times and supporting them through tough decisions. - Nil Gural, Polaris

I was drawn to biotech VC because I enjoy sifting through things, reviewing the latest and greatest science, determining if the science is viable as a business or not, and synthesizing all the information that I have learned to make an investment recommendation. There is never a dull moment! I continue to learn, be challenged in how I think, and connect as well as work with some amazing people, including entrepreneurs and scientists/clinicians. I hope that one day I will be able to look back and say, yes, I helped to develop drug X that was life-changing for X amount of patients! - Noelle Hutchins, Omega Funds

I didn't know what venture was until I worked on some translational projects during my undergraduate degree. I tried spinning out a delivery technology to reduce peripheral side effects of anti-epileptic drugs. During this project, I went through the UK biotech competition OneStart which was my first foray into the venture ecosystem. I had no intention of being on the other side of the table from where I was pitching our company at the time. The spin out didn't work out, so I went to get more experience at a biotech company and shortly after into an early-stage fund incubating companies emerging from academic institutions in the UK. Once I began working in venture, I was addicted to the wide variety of scientific concepts I could go through in one day, and the exceedingly high bar being set by the people I was engaging with. I feel privileged that I get to work with such talented founders and scientists every day. - Pablo Lubroth, Hummingbird

I started out in venture by co-founding a company during my PhD called NanoXCell Therapeutics with my twin brother Dan Lundgren (now at Rocksprings Capital) and Chris Lo (now at Enavate Sciences). We had the ambitious vision of trying to create a single cell CAR T cell therapy (inspired by a Carl June/Joe Fraietta paper) using a nonviral engineering approach. This was a great trial by fire introduction to trying to tackle a big problem with almost no resources. The company ended up dying, and many lessons learned (too many to write about here). Nonetheless, I got hooked on early-stage biotech and thinking thoughtfully about "crazy" ideas from the lab and trying to create an actionable plan towards value creation and capture (with a great team). In terms of initial misconceptions, I think one aspect I didn't fully appreciate early on is the non-linearity of the business we are in. We are fundamentally in the business of outliers. It's important to think deeply and repeatedly about what that actually means. - Patrick Lundgren, Hummingbird

I joined RA as an associate on TechAtlas (our internal research and diligence team who serve as subject matter experts and work closely with our investment team evaluating opportunities ranging from newco ideas to commercial-stage public companies) because I wanted to be exposed to everything I might want to do in biotech. Working in TechAtlas is like working at a hedge fund, a venture fund, and a consulting firm (where your only clients are RA's portfolio companies) simultaneously. Of all the cool things I got to do within TechAtlas, some of my favorites were helping our newcos make strategic decisions and diligencing early-stage companies. I love the challenge of spotting something awesome before anyone else sees its potential. I love the creativity needed to find the perfect application for a new technology, the rigor needed to evaluate new science, the clarity needed to shape an idea into a story that can inspire others. I even love the pressure of working on early-stage investments. I think there should be a certain level of anxiety that comes with the responsibility to help make big-impact decisions like selecting indications and targets to pursue, designing make-or-break experiments, and hiring the people who'll drive the company forward. But sharing that pressure with a team, all of whom are committed to realizing the same vision, is such a privilege. - Rebecca Silberman, RA Capital

My north star is wanting to contribute to the process of bringing interesting scientific ideas to patients who could benefit from them via therapeutics, medical devices, etc. I came to venture after spending time in academic research, helping academics form companies around their ideas, and investing long and short in publicly traded biotech companies. I hoped, and have since confirmed, that venture would be the ideal blend of getting in the weeds and contributing to strategy and development, while maintaining enough breadth to apply lessons learned in a seemingly non-linear manner. One misconception I had about venture was that it would be isolating, when in reality it's incredibly collaborative and team oriented. This is especially true at Novo Holdings, where on any given deal I have the opportunity to work with colleagues across our six offices (Copenhagen, London, Singapore, Shanghai, Boston, San Francisco). - Roman Camarda, Novo Holdings US

My journey into biotech investing began with my involvement in a student-run Biotech Investing Club at Weill Cornell. There, I delved into researching and understanding new technologies beyond my academic expertise. This empowered me to make informed trading decisions, particularly centered on predicting clinical trial outcomes for various companies. Over time, I curated and managed a diverse portfolio of biotech stocks, consistently monitoring market trends and executing trades with precision. Alongside this practical experience I completed my CFA Level 1 to grasp the intricacies of financial terms and concepts. As I neared the conclusion of my PhD and realized my inclination away from benchwork or pursuing a postdoc, I proactively networked within the life science venture community. This networking effort led me to an offer from Vertex Ventures HC. Through this journey, I came to recognize a fundamental misconception I initially held about biotech investing: I assumed it revolved solely around the science. However, it became evident over time that successful investment in this field hinges on three key pillars: science, team, and financing. Each of these components carries equal weight and significance in making informed investment decisions. - Sahil Chopra, Vertex Ventures HC

I joined venture from operating roles at both large companies (Davita) and startups (Synthego). Venture initially drew me in with it being one of the few places a background in both kidney care and gene editing could possibly be useful! Initially I had the laudable but naive perspective that simply selecting strong companies through diligence made for a good investment portfolio. Particularly in venture, so much more goes into the success of a fund - the access to investments you may have, how you operate on boards, timing of your investments, and more. The success of the investment really only begins with making the investment. - Shoman Kasbekar, Foresite

My interest in biotech venture capital stems from the unique opportunity to integrate science, medicine, and finance within a single role. I relish the process of acquiring extensive and indepth knowledge across various therapeutic areas. Initially, I was under the impression that a substantial background in finance was crucial for success in biotech venture investing. However, I have since realized that while financial acumen is essential, a significant portion of my responsibilities focuses on understanding the scientific and clinical evidence. - Suan Tuang, TCGX

My current role at Digitalis Ventures is my first full-time role in venture and investing, but stepping back, venture is the culmination of multiple experiences over the years:

(1) My first exposure to company building was in undergrad, when I worked to start a non-profit called Wishing Well that raised money for water projects in the developing world. Although it wasn't a biotech, the experience of working to build an organization from the ground up with a small, scrappy team has always stuck with me. (2) Science is more fun with friends, and collaboration was an enormous part of my PhD training. I was fortunate to co-develop a portable technology for single-cell sequencing that I worked to deploy in numerous collaborative projects that took me around the world and back. Venture capital is about the only job that lets me recapture the thrill of simultaneously working on projects that span multiple disciplines, diseases, and continents. (3) My time at nference showed me the opportunity for real impact in industry. Initially working part-time during my MD-PhD training, I was able to contribute to multiple projects across the biopharma ecosystem. After my MD-PhD training, I spent a year working to in-license a couple of assets in support of clinical trials in neuro-oncology at Duke. Through this experience, I was thrown into the deep end of drug development and company creation while working with the team of physician-scientists at the Duke Brain Tumor Center.

Now that I am working in venture, I am hooked. I get to spend my time thinking about the best ways to leverage the latest science to create the future of medicine – I can't think of anything more exciting. - Travis Hughes, Digitalis

3. What was the first deal you worked on that resulted in an investment? What are the biggest lessons you learned from this experience?

The first deal I did as an associate was Avalyn. What I learned is to try to figure out what you're looking for (or not looking for) before you look for it, to make friends before you need a friend, and to be really persistent when you think you've got something interesting. - Alex Loftis, Vida

The first deal I worked on that resulted in an investment was in an ophthalmology company called EyeBio (in which VVHC led the Series A extension). The biggest lesson I learned was how important it is to quickly establish a solid investment thesis as your north star, and to be disciplined about triaging new information in the context of that thesis while moving through various aspects of the diligence process (i.e. scientific, clinical, legal/corporate) - Amanda Chen, Vertex Ventures HC

During my VC fellowship, I had the pleasure of supporting brilliant colleagues <u>Colin Walsh</u> and <u>Phil Digiacomo</u> as they were working on the Series A investment for what became <u>Entact Bio</u>, a company built on chemical biology expertise utilizing deubiquitinases (DUBs) to stabilize proteins via heterobifunctional chemical modalities, rather than degrading them via popular E3 ubiquitination enzymes often found in PROTACs. Working alongside the team, I came to appreciate the threading of the needle needed when diligencing within a potential emerging sector – since the time of our investment, many more companies have been launched exploiting DUB biology for new therapeutic strategies! - **Artie Arumov**, **Qiming**

My first deal exposure was with ReAx Biotechnologies from Ray Mollering's lab at the University of Chicago. This company was created based on Ray's academic work in advanced protein ligation and novel chemistry methods. The biggest lesson from that experience was ensuring strategic alignment across key stakeholders before approaching the investment committee for a decision. The key to receiving a yes to any investment request is alignment across the deal diligence team regarding their evaluation of the technology, from the lead to every supporting member of the diligence team. - Danjuma Quarless, AbbVie Ventures

My first deal was Dren Bio's Series A, where I had the opportunity to partner with CEO Nenad Tomasevic and team. I was excited about the lead asset, the CEO's past work, and the possible upside on their platform. The company has since exceeded expectations in every axis I could imagine. I think this comes from Nenad and team's absolute clarity on what needs to get done, which results in the speed and capital efficiency that the company has enjoyed thus far. It has become a trait I look for in founders. - David Yang, Lux Capital

BioAge Labs was the first deal I worked on that resulted in an investment. OUP participated in BioAge's \$170M Series D financing announced in February 2024, and I worked on this deal supporting Mitra Miri, a principal on our team, as well as Matt Cohen, one of OUP's managing partners. BioAge is a clinical stage company developing an oral apelin receptor agonist in combination with incretin therapies for the treatment of obesity. Venture is definitely a career where the best way to learn is by doing, and sprinting on this fast-paced deal facilitated a huge amount of learnings in a very short timeframe. This includes the diligence, of course, but also all the dynamics that come into play after you build the conviction to get to a "yes" internally. A

critical element, especially in fast-paced deals, is to run a rigorous process you can be proud of, and working on this deal with Mitra and Matt was an opportunity to learn that in action. **- Harry Won, OUP**

The first deal I worked on was to in license a thyroid beta agonist for NASH from a Japanese pharmaceutical company. My thesis was that the molecule had better properties compared to the lead competitor in the space. Coming from behind meant convincing investors and strategic partners that there was meaningful differentiation despite the early stage of the molecule. There were meaningful challenges that I had to overcome to get first my employer to take a bet on this investment, and later Pfizer partner with me. There was little structure, training, or support in my first investment role, and it would've been easy to not take my own project seriously. However going back to first principles, and knowing where I eventually thought I would be helped shape the way I treated my time working on this project. It meant that I maintained being organized, always asked myself why I was doing something, and establishing a network of biotech colleagues and potential mentors to help me push myself to the next stage of my career. - Jason Wang, Frazier Life Sciences

I started my full-time career in biotech investing in mid-2021. Shortly after I joined, we made several investments in public companies based on multi-year theses. Many of these theses have ultimately played out successfully, but they were nevertheless affected by high volatility in mark-to-market valuations during the biotech bear market that occurred in the interim. Macro is an important short-term consideration when considering investments in both public and private companies. However, this experience illustrated to me the necessity of maintaining a long-term view of the fundamentals, especially as market conditions can be highly dynamic. - Kevin Li, Frazier Life Sciences

After almost 10 years in various venture internships and roles, I can definitively say that I've learned twice from much of the deals that failed than the deals that resulted in an investment. So, sharing some lessons from the so-called "failures": (1) Always replicate key experiments in an independent lab, this is never money or time wasted. (2) You will spend tons of hours working on ideas and diligence with founders, only to have them turn down your term sheet and go in another direction. This is not a loss. The fraction of time spent during ideation and diligence pales in comparison to the hours that would be required from Seed to exit. You've spent some time 'dating' the founder to figure out that you're not on the same page for 'marriage' and learning that is hugely valuable. (3) Just because a deal falls apart doesn't mean you have to stop rooting for science/team that you were excited about. Careers are long and people remember when you are in their corner, especially when you don't have to be. **- Lauren Mifflin, Frazier Life Sciences**

While I was fellow, I was part of the diligence for Vida's investment in Scorpion Tx (Targeted oncology) and as I started at Atlas the first seed venture creation project I supported was Chroma Medicine (Epigentic editing). Both showed me that building successful biotechs is as much about finding great science as it is about working with great people. - Maurizio Fazio, Atlas

The first deal I worked on that resulted in an investment was Crossbow Therapeutics; a company developing TCR mimetic antibodies against intracellular targets. At the time we met the company, we were already forming a hypothesis around opportunity areas in cell therapy at Polaris and Crossbow was a wonderful fit in terms of what we considered the next frontier in cell therapy. Meeting the stellar team only strengthened our conviction. Crossbow is a company pursuing an ambitious idea, and fittingly has an amazing team behind it that is able to balance innovation with execution. We look forward to sharing some of the exciting developments later this year! - Nil Gural, Polaris

The first deal I worked on that resulted in an investment was Boundless Bio. What drew is to the investment was strong biology coupled with an exceptional CEO. What I learned, particularly in early-stage venture investing, is that while you can't precisely forecast how the science will evolve post-investment, betting on the team pays off. Luckily, that bet paid dividends with Boundless Bio! - Sahil Chopra, Vertex Ventures HC

EpiBiologics was the first deal I worked on at Digitalis that resulted in an investment. Lessons learned:

- Swing for the fences . . . once you know your strike-zone. You have to look at a lot of pitches before you can recognize the ones worth swinging at. Investing is all about pattern recognition, so it important to see a lot of deals early on.
- Eventually you have to run an experiment no investment is absent risk it's venture capital after all but the goal is to understand the risk-return profile you are underwriting with an investment. You can always ask more questions, but eventually you have to take the plunge.
- **Sometimes you just know** "You know how to tell a bad deal? The ones you need to diligence." Anonymous VC Sage.

While it is essential to be systematic and principled, there are times where intuition is all you need and you just do everything you can to get in the deal. Those are rare birds, but ones I am always looking for. - **Travis Hughes**, **Digitalis**

4. What are some factors that get you excited about a company or company build? Is there a mental checklist or model that you construct during diligence to gain conviction about an opportunity? Any obvious red flags?

For me, any biotech company that is bringing forward new technology or pipeline projects that will result in *truly* differentiated products for patients is exciting. Gaining conviction that the company and science is ready to do this with *reasonable* resources, both time and capital, is often the biggest hurdle in an investment. 'Reasonable' is obviously almost completely dependent on both a firm's investment strategy and the company specific investment thesis. To clarify – At MPM BioImpact, it's absolutely not an issue if early-stage companies haven't figured

out their product development path – it's often exciting to partner with companies to put this path together. - Alim Ladha, MPM

At VVHC, we focus on both biotech drug and therapeutic medical device investing. Since all deals are different and unique, it's hard to comprehensively represent the diligence process with a rigid checklist. We follow a philosophy centered around three pillars, which has been previously discussed by our Boston-based Managing Director, Christine Brennan. A brief summary here is that we 1) look for good science that is differentiated and has potential to be clinically meaningful, 2) a management team that is either experienced or has the proper support to navigate the challenges of biotech/medtech product development and company building, and 3) a financing plan that moves the company through critical milestones that the investing community recognize as value-creating and on the path toward new medicines for patients. - Amanda Chen, Vertex Ventures HC

For a therapeutics company (where 5AM spends most time), I get excited when I can articulate how a company's technology or novel insight enables them to uniquely address a high unmet need area. While every opportunity is totally different, being able to answer the differentiation/"why now" questions unlocks some high-level "checklist" items for a platform or asset company: 1) Balanced biological vs. technical risk?, 2) Does the development plan create meaningful value for the next financing?, 3) Compelling exit path?, 4) Are the right team members and investors at the table to maximize success? ?, and 5) If the product is approved, does it make a difference to the lives of patients?- **Aniqa Tasnim**, **5AM Ventures**

I feel that every deal and company build opportunity truly is different from one another, and thus it's difficult to systematize things into a checklist. However, core factors that I've found showing themselves time and time again across "successful" deals are 1-2 leaders within the company standing out with a genuine passion and drive for solving the problem at hand, and not shying away from answering questions, even if they don't have the answers. **Just do good work** and don't speak in circles! Combining these traits with an exciting translational biology hypothesis, ideally one that's truly emerging and on the cusp, and can improve upon patient need, gets me really excited to dig into diligence. **- Artie Arumov, Qiming**

The exciting factors are a technology's or application's raw potential, especially in novel therapeutic drug platforms. New company builds are challenging in the beginning because the team doesn't have the resources, corporate structure, or maturity of an advanced company, which means investors and board members must contribute heavily to their development in the beginning. However, a much higher degree of aspiration, optimism, and excitement exists as the company attempts to succeed on a grand scale. A red flag would be a founder or executive team that signals a diminished ability to rely on their investment syndicate or scientific advisory members for insights. Capital inefficient companies would be a massive red-flag in this market. - Danjuma Quarless, AbbVie Ventures

Within therapeutics, one phenotype of a company I get excited about is a platform technology that unlocks a specific target(s) that otherwise would be difficult to address. Platforms are of course exciting, but one pitfall is when they are generally useful but not meaningfully differentiating for a specific, high-value target. It's important that from Day 1, there is clarity on what target / type of targets a platform can be useful for. Take Relay Therapeutics' platform for molecular dynamics, which is a useful tool for identifying allosteric inhibitors. The team was able to map this platform capability to a set of fast follower, best-in-class molecules in onc such as their FGFR2 inhibitor (relative to Pemagitinib) or Pl3Ka_mut inhibitor (relative to Alpelisib). -

David Yang, Lux Capital

VC exists as an asset class to return capital to our LP investors, and it is this fiduciary responsibility that ultimately drives the way we think about exciting investment opportunities. We anchor to the exit (whether pharma M&A or going public) and what we think this company could be worth in success (for us, focusing on the lead program(s), not the platform). For therapeutics, this tracks well with magnitude of potential clinical impact, which is the source of my passion for this work, as it is for most biotech investors. What is the unmet need and how would this therapeutic transform the current standard of care, if any? A non-exhaustive list of considerations:

- 1. How validated is the target and the proposed MOA (validated disease driver or totally novel target?), is the modality the best approach for a given indication (instead of having a promising technology looking for a problem)?
- 2. How compelling is the preclinical data (quality of models?), how developed is the chemistry/PK/potency?
- 3. Does the clinical trial design make sense, is it possible to demonstrate PoC in a short time?
- 4. What is the competitive landscape, are there regulatory challenges or tailwinds? How easy is the drug to manufacture?
- 5. What are the value creating milestones this financing purchases, are they enough to get investors excited the next go around? Is there enough runway to get that raise done? These points are especially important in tough financing environments.
- Last and most importantly, team is critical. Are there experienced drug developers
 around the table, whether at the helm or deeply involved as advisors? Harry Won,
 OUP

I don't think it's always possible, nor fair to the companies, to boil down why I start to gain conviction in a particular company. I've become a bigger believer in 'the prepared mind' – that is to say the more you understand and think about an emerging modality or interesting piece of biology the more likely you'll be able to quickly and appropriately become excited when the right opportunity presents itself. More recently the companies I've become excited about have tended to be tangentially related to ones that we're very recently interacted with. Time will only tell is that's a prepared mind or recency bias, but there are interesting subsections of biology which can helpful inform others. - James Buxton, NEA



I mainly work with therapeutics. There are several common checklist items:

- 1. Common items to immediately check for are market size, biological rationale, preclinical efficacy and safety, PK/PD, and finally clinical efficacy and safety
- 2. Ultimately there are usually 2-3 key diligence questions that you need to answer and that takes 80% of the time compared to the rest of your check list
- For therapeutics with reputable teams and companies, usually there's not an obvious red flag. It's more about the time for them to generate data that allows you to develop conviction that holds an investor from investing now versus in a later round – Jason Wang, Frazier Life Sciences

I like teams that do good and thorough science. While mitigating risk is an important element of our work, I gravitate toward companies that are not afraid to take biology or development risk if required to meaningfully advance the standard of care. I am less excited by projects that appear relatively de-risked but that have unclear or minimal clinical benefit over existing therapies. When reviewing opportunities, I find lack of transparency or candor problematic; information that is not shared is often more important than information that is shared. I also am a stickler for rigorous scientific and statistical methods. - Kevin Li, Frazier Life Sciences

Every project is different - a compelling therapeutic seed build can start from a clinical stage asset or from a technology idea on paper. There is no fixed starting point or universal data package & diligence recipe. What is critical for me is to 'see the drug opportunity' that a platform or asset could uniquely unlock, supported by a compelling data rationale of 'why it will work'. In therapeutic discovery we are always chasing the intersection of the right drug, for the right target, for the right patient, with the right clinical trial. - Maurizio Fazio, Atlas

There is no "formula" to identifying a great company and there is something to be said about experience and instinct. Overall for me, it starts with a few high level questions – beyond that, I try to be open to surprises: (1) Am I excited about the science / technology? Is it serving an unmet need? (2) Is this a stellar team that can execute on their goals? Can we work together? (3) Is there a well thought out development plan? (4) Is the team thoughtful about the capital needs to execute on their milestones? (5) How can we, Polaris, help them succeed, beyond being a source of capital? - Nil Gural, Polaris

Things to get excited about: Does the company have a technology/product that is differentiated? Will their product or drug be a gamechanger in a particular disease and/or target indication? Is the overall science/ biology validated? Does the company have a mgmt. team that can execute? Do the timelines make sense, and what are the overall projected budgets and costs with the current fundraising? And, of course, does the company have a viable exit path? Is there a growing investor sentiment, i.e. how hot is this deal? Red flags: Technical risks (foreseen toxicity, difficult to reproduce academic laboratory results), regulatory risks (unclear efficacy endpts), clinical developmental path is not well defined - **Noelle Hutchins, Omega Funds**

There are always hundreds of technical, commercial, or team-related questions you can ask a company at any given point. I write down as many as possible and then select the top 20% that are critical to deciding if we want to move forward. If the answers to those are favorable, we write the next batch and select the most important ones, and so forth. This has helped me come to conclusions faster which is beneficial for everyone. Every company and founding team is different, so we adapt our line of questioning for each one accordingly. A must for us is evidence that founders can attract a world-class team, demonstrate a measure of unreasonableness, and have an incredible sense of urgency. **- Pablo Lubroth, Hummingbird**

Number 1 is the team, especially at earliest stages. Ideas/technologies/market can change (often does) as a company matures from pre-seed/seed, but the core team is relatively static. So the key factor is whether I have conviction in the ability of the founders to build a generational company. Do they have an unreasonable sense of urgency? Are they headstrong while also able to work well in teams? Do they have a remarkable level of domain expertise? Are they "outliers"? At hummingbird we also like founders that are on a mission to prove others wrong, and so by definition they have a differentiated view of the world which ideally translates to the potential for a category-defining company. There is of course the boiler plate checklist on: market risk, technological risk, biological risk, clinical risk, timelines, capital needs, exit opportunities, etc. And obviously these things are important to diligence thoroughly (mainly because it allows for an in-depth assessment of the team quality). - Patrick Lundgren, Hummingbird

During diligence, I try to remember that making an investment is as much a decision of "when to" as it is "whether to." I ask the usual questions on biological rationale, market opportunity, and valuation. But I also focus on the key milestones achieved by this raise and whether this is the right time to invest, or if it would be more prudent to revisit at the next raise, even if that would mean investing at a higher valuation. I map the company's development milestones onto the upcoming catalysts and trends in their field to try to understand what headwinds/tailwinds exist outside the company's control. I try to put each company's approach into the context of the history of their field to understand what technical/scientific breakthrough unlocked their solution (and whether another breakthrough is on the horizon which will totally change the competitive landscape). When I find a company at the right stage of development for us to invest and poised to capitalize on an opportune moment in the evolution of their field, I feel like I've found something special. - Rebecca Silberman, RA Capital

Thanks to a relatively challenging IPO market, companies have largely been forced to spend more time building their narratives and datasets in the private markets. I get excited by strong assets that provide good fit relative to the unmet need they aim to address. Good fit can come in many forms (e.g., genetic validation of a target, optimal dosing regimen, formulation), and on the flip side of that an obvious red flag would be bad fit (e.g., patients have mobility issues, and your therapy can't be administered at home). - Roman Camarda, Novo Holdings US

My initial excitement for a company usually stems from the science and the data behind it. Alongside that, my mental checklist includes evaluating the team, their milestones, the unmet

need they're addressing, and the potential for value creation. A major red flag for me is when someone tries to oversell the data—it's a real pet peeve of mine. Another glaring warning sign is if the pitching team seems out of touch with the landscape and recent developments in their field. Being well-informed is key in this game. - Sahil Chopra, Vertex Ventures HC

Mental checklists, while helpful, exist to be broken. There isn't a single process that works universally across deals. I first try to orient around characteristics of the company that may outperform by an significant amount / order of magnitude. This could involve a step function change in our ability to drug a target, or a growing data moat that may fuel a company to outpace competitors. Biotech is an industry that rewards primarily first in class or best in class. In addition, I am excited by companies that can clearly hit value-inflecting milestones - this sounds straightforward, but numerous companies are financed to uncertain or challenging end goals, crippling further financing. - Shoman Kasbekar, Foresite

My focus is on therapeutics, and I ask myself the question "If this company were to succeed in developing this drug candidate into an approved product, why would a doctor prescribe it?" Asking this question early on in my diligence process helps me contextualize the investment opportunity and identify key questions I need to dig into. - Suan Tuang, TCGX

I spend most of my time focused on therapeutics companies. Here is a non-exhaustive mental checklist:

- Amazing Science There are countless variations on this theme but tl;dr the science has to be compelling. No matter what the pitch, I must believe it is an experiment that is worth running and will likely succeed in both the lab and the clinic.
- **Technical Advance** Does the technical achievement leave me awestruck? Here, I am always looking for elegant and non-obvious solutions to wicked hard problems that result in a deep technical moat and highly defensible IP.
- **Opportunity for Impact** Is the problem real and worth solving? If the problem is over-stated or the benefit to patients is unclear, it is hard for me to get excited.
- Problem-Solution Match Is it this the right tool for the job AND the best job for
 the tool? It seems simple, but it is often the most important thing I am looking for,
 and there are a lot of ways that this can be out of balance. While this is something
 that companies are always fine-tuning in flight, I focus heavily on how much time a
 team has dedicated to thought experiments and pre-design prior to pipetting.
- **Novelty** How does the approach compare to what others have done/are doing in the space? There is a sweet spot here: not so incremental that it is essentially duplicative, but not so far out that it is believable.
- Line of Sight Is there a clear path to multiple value inflective data points that are
 well-aligned with subsequent rounds of financing that culminate in new medicines?
 I am looking for a sensible and focused plan to advance the lead programs to the
 clinical while also supporting additional creativity and discovery.
- **Top-Flight Team** You are investing in people more than anything, so I am looking for people who have the necessary experience, creativity and judgement to



make the magic happen. Is this a team that has gone/can go the distance? Is the team the right size? Is this a team I will be beyond excited to work with for 5+ years?

Red flags:

- Technical Myopia A disproportionate focus on technical milestones without a
 clear sense of eventual application(s). This is one of the issues I often see with
 platform technologies that have access to an essentially unbounded application
 space. When anything is possible, it makes the choice of the best, first application
 even more critical (and so much harder), so I always encourage people building
 platform technologies to do so with a laser focus on what their technology uniquely
 enables.
- Science experiment Great idea . . . for an academic lab. While there is often not
 a clear point to transition a project to a company, I look for science that simply can't
 go any further in academia. In general, I am looking for mature academic science
 in need of a dedicated team and capital infusion for engineering and optimization
 ahead of commercialization rather than large-scale data generation or discovery
 efforts.
- Buried Leads Like it or not, you have to love the lead program. It is important for a company to have a deep pipeline, but if I only like the third program, it becomes a difficult investment to underwrite.
- Platform, Pipeline Mismatch If a discovery platform wasn't necessary to develop the pipeline programs, it always raises questions about clarity of thinking and capital efficiency. Companies pivot all the time, but it is important to understand the origin story, the magnitude of course correction, and whether it has left the company in a better position. Travis Hughes, Digitalis

5. Using your mentors as examples, are there any traits or skills that you have tried to develop to become a better investor or creator?

I would say the people I respect the most as investors are transparent, thoughtful, and at their core really enjoy learning. Not that this is a prerequisite, but I would also say many of them also have had meaningful professional and / or personal experiences outside of VC and have a good sense of perspective. - Alex Loftis, Vida

I've had the opportunity to work with excellent mentors in my career – through that, one trait has been quite consistent: a willingness to say, "I don't know". This willingness and self-awareness enable an intensely logical mode of problem solving that, somewhat paradoxically, leads to much deeper understanding than simply relying on 'established' facts. - Alim Ladha, MPM

I am very grateful to work with several experienced colleagues (Christine Brennan, Lori Hu, Sahil Chopra, Shawn Fu, Jeff Schlosser, David Van Meter) that uphold a very disciplined and

objective decision-making approach that is both rooted in intuition and data. There are so many exciting opportunities in healthcare/life science investing, and funneling energy toward diligence on deals that we are most likely to get across the finish line is not only strategic, but imperative.

- Amanda Chen, Vertex Ventures HC

I've been fortunate to have awesome mentors that all have distinct styles and have paved the road to their success in very different ways. A few traits/skills that I'm working on: 1. Getting out of my comfort zone (in a lot of ways), including reading outside of my wheelhouse (e.g. NEJM, Nature Biotech), 2. As an early-stage investor/company creator, engaging with late-stage private/public investors, equity research analysts, and bankers – their views on what creates value in the clinic and commercial markets are incredibly valuable, 3. Being present (consider turning off email/text notifications during meetings!), and 4. Being empathic, especially to founders, management teams, and scientists, whose jobs are incredibly challenging. - Aniqa Tasnim, 5AM Ventures

Balance is important to success in investing and company building. I continue to learn from Bruce Beutel about the importance of the day-to-day activities needed for success within a biotech company, and the constantly evolving scientific planning & scenario mapping happening, as one example, and certainly one that I leverage in both our company build efforts as well as in supporting portfolio companies as a board observer. The plan will inevitably change multiple times over (if it's not, then you've got another problem!), based on experiments and emerging data, and being able to continue handing off the baton from one scenario to the next without losing momentum is critical. Anna French has taught me to not be afraid of thinking outside the box and in fact owning a personal brand of scientific creativity, but importantly never at a high level and always with an appreciation and understanding for the scientific nuance within the field of interest. There's a lot of crowd sourcing for the same sets of drug targets and therapeutic approaches, yet often the best discoveries and inventions require a small subset of people to have taken the initial risk and pushed ahead. Handing off the creative baton while keeping the pace is key to success! - Artie Arumov, Qiming

I've been fortunate to learn from an incredible group of mentors who have all shaped my growth as an investor. Beyond the table stakes aspects of venture (e.g., diligencing deals, evaluating teams, building a broad *and* deep knowledge base across therapeutic areas), what especially resonates are the human element of our profession. The importance of building non-transactional relationships, whether investors, operators, or support staff. Having the humility and empathy to learn and listen first when engaging with entrepreneurs as they are doing the actual hard work of developing the therapeutics we all hope become new medicines. Showing integrity in all your interactions first and foremost because it is the right thing to do, but also because the biotech community is very small! My special thanks to Anurag Agarwal, Matt Cohen, Bill Harrington, Stefan Vitorovic, Arjun Goyal, and Colin Walsh. - Harry Won, OUP

I've learnt a huge amount from Ali Behbahani and Ed Mathers who have invested through multiple economic cycles. While they each have their individual investing styles, they're both fantastic at understanding (and communicating) how time, risk and reward are intertwined when



assessing a new opportunity. Specifically, I've tried to spend more time thinking about how risk can quickly compound when a company is addressing several unanswered questions – mechanism, delivery, patient population, clinical development plan for example. **- James Buxton, NEA**

To figure out an investment style and to do more reps after I've found it. Some investors focus on strong networks for deal flow, others on deep personal diligence, others still on a gut sense. I've been exposed to all of these styles, and I need to develop my own or blend of these. - Jason Wang, Frazier Life Sciences

I find the most inspirational leaders are those who treat their colleagues and peers with respect, honesty, and good faith. Humility is a prerequisite for our work, as drug development is hard and often humbling. Also, no position is too senior to engage with data and do the diligence. **- Kevin Li, Frazier Life Sciences**

VC is a trade we learn by active apprenticeship and the past three years at Atlas have been a permanent osmotic gradient of learning on so many fronts. Just two highlight a couple of examples: From Jason Rhodes (Atlas Partner): Clear, strategic, and goal (vs. activity) oriented communication; Use capital & time exposure as a scale to normalize scientific risk-reward. From Bruce Booth (Atlas Partner): Seek and invest in real longitudinal relationships with people you admire across the whole ecosystem (academia/pharma/biotech/investors); building a community will help you build better organizations. - Maurizio Fazio, Atlas

There is an often under-valued "people aspect" in venture that I think about often. People who I look up to in the business build long-lasting and loyal relationships, support their entrepreneurs especially through the hard times, keep an open line of communication at all times and treat others with respect. That's the kind of investor I aspire to become. **- Nil Gural, Polaris**

Mentorship can come in various forms and outlets and for this reason, you can't be afraid to take golden nuggets from anyone, this includes the Partners that I have interacted with Omega Funds. However, I have found at times, my best mentors to be my peers in this industry. Not only do they keep me honest, but they are some of my best cheerleaders and challengers. Should I formally mentor a junior person, I will be transparent and ensure that I spend the appropriate time necessary for them to meet their goals and see overall growth. - Noelle Hutchins, Omega Funds

At Flagship I learned that you need to be able to balance traits that are basically conflicting. You need to be a "paranoid optimist". You need to be idiosyncratic, but also able to work well with teams. You need to be very stubborn, but also open-minded. Another piece of advice that I took to heart is that if you want to invent the future, specificity is more important than accuracy. I think developing these skills is important, and I look for these things in people I want to back now at Hummingbird. It's been interesting to intersect these perspectives with the way

Hummingbird thinks about founders (a firm that has been thinking deeply about remarkable founders and companies for 14+ years). - Patrick Lundgren, Hummingbird

I am amazed by how quickly and decisively the RA team takes action in the face of threats to our sector. Confronted by the Inflation Reduction Act (IRA), which enacts Medicare price controls on small molecule drugs 9 years after approval and biologics 13 years after approval, RA's leaders have consistently rallied the biotech community to speak out in its own defense. They've educated decision makers in Congress and beyond on how to quantify the true value of biotech, published a recent article on how to protect the future of US innovation, and launched a non-profit called No Patient Left Behind which advocates for reforms and advises policy makers on how to enable patients to actually access the medications they need. For anyone who also cares about defending innovation and ensuring that our work isn't wasted supporting drugs through approval just for them be kept out of patients' hands, you can sign up as a First Responder on the NPLB website to stay in the loop and lend your support (also, there's a program just for college and graduate students called NPLB Fellows).

Speaking out isn't necessarily in my nature. When faced with some new and unexpected challenge, my first instinct is to step back and observe, to wait to see how the situation is evolving before deciding how to react. Watching my colleagues dive into these conflicts as they unfold to try to help all of us avoid their worst consequences, I can't help but see parallels to the work I do every day. The same conviction that compels me to argue in favor of early-stage investments—even when they're risky, even when they're challenging—to help RA play a role in bringing a new medicine into the world compels me to take action to right wrongs as they unfold around me—even when it feels easier and much less risky to just be a bystander. The reason I find it so dismaying to see other funds remain on the sidelines, seemingly content to invest as long as the policy framework makes biotech investing profitable but doing nothing to actually preserve that framework, is because I'd also prefer to not have to step out of my comfort zone and to stand up for biotech. But, because my colleagues at RA refuse to be bystanders, I won't either. As with investing, I'm still learning how to take action when called upon and am glad to have a team to learn from. - Rebecca Silberman, RA Capital

I have to give a shout out to my high school biology teacher and one of my longest standing mentors, Jim Johnston, who deserves full credit for putting me on the science path in the first place and continuing to support me ever since. Jim has taught me the value of being humble and curious, staying hungry, and having people and ideals in my life that I would gladly run through a brick wall for. I'll also give a nod to Howard Marks, who I don't know personally, but his suggestion to be mindful of others being greedy vs fearful has been continuously applicable.

- Roman Camarda, Novo Holdings US

The 3 traits that I have learnt from my mentors are:

- c. Listen more and speak impactfully. It's not just about talking; it's about the quality and impact of your words
- d. Maintain a long-term vision; resist the allure of investing in trends or fleeting fads. Substance over hype, always



Always back your assertions with solid data. It's the foundation upon which wise decisions are built - Sahil Chopra, Vertex Ventures HC

I'm generally an optimistic person, but where to apply optimism and skepticism is a muscle every investor must train. Being overly critical of the risks in a venture investment can be just as dangerous as being overly optimistic about the opportunity - after all, venture investing is a power law game. I've been lucky to work with colleagues who are keenly trained on identifying which risks/opportunities matter the most in the context of a certain type and stage of investment. - Shoman Kasbekar, Foresite

One quality I admire in my mentors is intellectual humility. This single skill allows one to acknowledge the limits of their knowledge, which mitigates overconfidence and instills a continuous learning mindset. - Suan Tuang, TCGX

Problem Selection – choice of problem is the most important thing in science - everything else flows from that. This is one of the most important lessons I learned from Jack Strominger (I spent a year living with Jack during my PhD). As an investor, I am always striving to ask the right question(s) of myself and of companies: What would make the biggest impact? Am I spending my time in the right areas? Is that the best approach or lead indication?

Curiosity - More than anything – curiosity, passion and excitement about science and medicine are what motivate me in VC. Over the years, I have spent a lot of time working with kids and even more as a parent – kids see the world differently and get excited when they learn new things. I love the opportunity to just geek out with brilliant people who change the way I see the world and make me say: "That is just so cool!"

Attention to Detail – Alex Shalek, my PhD advisor at MIT, always pushed me to higher standards on the little things that can make a big difference - I can't count the number of times I revised minor details (e.g. re-aligned figure legends, changed font sizes, or adjusted color schemes). While it was frustrating at times, I wouldn't trade this experience for the world. It is rare to find people who care enough to expect next-level excellence from themselves and the people around them.

Empathy - I strive to bring a lot of empathy to the table as an investor – everyone we talk to is brilliant and working on cutting-edge science. It is easy to lose sight of this as an investor. I think it is critical to periodically pinch yourself and remember what a real privilege to be an investor and that at the end of the day, we are all on the same team.

Pragmatism – Peter Lebowitz is someone I was fortunate to work with while at nference and greatly admire. From Peter, I came to appreciate key differences between problem-solving in academia and industry. In academia, complexity has a certain cool factor and is often necessary to dissect mechanistic subtleties. In industry, solutions should only be as complex as absolutely necessary. Ultimately, complexity leads to delays and time is of the essence because patients can't wait.

Patient Focus – At the end of the day, it is all about patients - making things that go into people's bodies to make them feel better. Period. The patients I have been fortunate to care for over the years serve as a guiding and grounding force. **- Travis Hughes, Digitalis**

6. If someone decides that VC is for them, any advice on finding a job in this environment? What are 1-2 things you would recommend doing to be proactive?

Do a fellowship! You won't know until you try it. Also remember there are other career paths that give you exposure to what you do as an associate in VC. I think it's really important to talk to as many people as you can before deciding what you might pursue after grad school – use those alumni networks. - Alex Loftis, Vida

Certain investing strategies will speak more to some people than others. If you are looking for a job, try to learn about firms' investing strategies. See which strategies best match how you view the world. Alignment there will often make you successful in the hiring process and on the job. - Alim Ladha, MPM

I think that strong relationships and intellectual curiosity are two important ingredients for any VC. So, my advice is to build your network and to learn broadly and deeply about the space that you are interested in investing in. Within that – do what feels authentic to you. Here are some suggestions based on what worked for me: if you're in school, try to sign up for internship programs or hackathons or workshops that are hosted by organizations you'd like to learn more about, and attend networking events featuring alumni that work in these spaces. Pick the brains of people who are in roles that you would like to know more about, and reflect on what does or doesn't resonate with you. Connect with your peers – many of my most meaningful connections in the industry are my co-interns from various extracurricular programs I explored during grad school. - Amanda Chen, Vertex Ventures HC

Form a thesis on a few areas of biotech that you're excited about (e.g. What are the limitations of current non-viral delivery mechanisms? What would get you excited about a new delivery technology?). It's great practice for the role, and as you take informal and formal interviews, your enthusiasm and clarity of thought will shine through. - **Aniqa Tasnim, 5AM Ventures**

Networking is of course key, but in the right context. When I meet with folks, irrespective of if they're already in VC or looking to get into VC, I often try to learn something from them to take home and study further. I'm always impressed when coming out of a meeting with an aspiring investment professional whereby they've taught me either about something I didn't have an appreciation for, or better yet, something where I thought I knew it all yet clearly, I didn't! If you're looking to break into VC, it's important to build perspective on at least 2-3 different scientific topics end-to-end (state of affairs on technical side, competitive biotech side) and ultimately having an opinion on what you would, or wouldn't do, in the respective sector of interest. Choose something that's within your technical background, but also at least 2 things not! And don't just re-hash the first 1-2 sections of the latest review article – go deep, get technical, and most importantly own an opinion on what to do with the information (e.g., investing in XYZ, or building a company that looks like ABC). - Artie Arumov, Qiming

Be tenacious and ready for a challenge. The career counselors from my MBA program at Kellogg shared this advice, and I 100% agree with them. Almost all roles in venture capital, investment banking, or private equity (at top firms) are determined by a partner or managing director's relationship with a potential candidate. It's not impossible, but it's less common for an individual to cold submit a resume that leads to a job. This means that each person wishing to join venture must intentionally build strong relationships, which takes time. I'd recommend attending as many ecosystem and investor events as possible (leverage student discounts or a local nucleate chapter) and ensure you understand the market and current state of investing so that you're ready when you get a shot to interview. **- Danjuma Quarless, Abbvie Ventures**

One advice I would give is to gain a very deep understanding of two different areas of biotech. This could be a thematic area such as radiopharmaceuticals or therapeutic areas like cardiometabolic. Beyond understanding the science, I would also try to understand what is top of mind for the insiders (e.g. upcoming major catalysts) and develop opinions around them. This allows you to build a network within said specialty areas, demonstrate the capability to go very deep, and have rich debates around specific opinions within specific areas. - David Yang, Lux Capital

The very first step should be to become better aware of the industry and what is going on. Regularly reading the biotech news is a great way to build your knowledge base and to have something to contribute to conversations with VC (Endpoints is probably the best but requires a paid subscription; Fierce Biotech is also great – signing up for their daily newsletters is the move). For a graduate student, it is critical to then really understand whether VC is something they would enjoy. To that end, coffee chats with VCs are great to learn more about the career and begin to build your network. My experience has been that people are extraordinarily generous with their time, particularly to those just starting out. To go even deeper, completing a venture fellowship (or multiple) would be the next step (Nucleate's Michael Retchin has compiled a helpful resource that is a great place to start looking). Almost every investor I know has a unique series of experiences that led to launching their career in VC. Keeping this in mind, I would close with the importance of being open to a wide variety of career paths that allow you to collect various skillsets that make for a good investor (e.g., consulting, equity research, joining a startup). - Harry Won, OUP

When you're having conversations with people at funds be proactive at digging beneath the surface level information you'd find on a website to work out how each of them differ. It's important to get a grasp on the types of work, level of autonomy and immediate responsibilities that you'll receive. As you build a better understanding of the day to day job you'll become a more attractive candidate to hire and one that will ask more insightful and thoughtful questions. - James Buxton, NEA

There is no substitute for doing the job. There are now several venture firms that offer summer internships that provide exposure to the day-to-day activities in this world to current students. Equally important, you can get a sense of whether you really "like it" which is important to long term career success in venture capital. - Jason Wang, Frazier Life Sciences

Unlike banking and consulting, investment firms may hire irregularly and often on an as-needed basis. Finding the right role can require being in the right place at the right time. For those considering a career in investing, I encourage seeking conversations with people of different personal and professional backgrounds and at varying career stages. When I was starting out, this helped me identify and vet potential opportunities, as well as solicit career advice, which was invaluable to me as I was considering a future in clinical medicine vs. Investing. - Kevin Li, Frazier Life Sciences

Fellowships, fellowships, fellowships. Over the past decade there has been huge growth in the number of fellowship/internship opportunities available to graduate students. Many biotech groups (e.g., Harvard Biotech Club, MIT Biotech Group) actually allow students from anywhere to sign up for their listservs, so would encourage those as great sources of information. Also, don't conflate the learning experience from student-run organizations with what can be learned from a VC fellowship – having had the opportunity to be in a fund's offices and overhear the small conversations in between meetings taught me as much as an entire year of academic VC coursework. - Lauren Mifflin, Frazier

Take advantage of any opportunities to gain relevant experience beyond your scientific skills. If you're still in grad school, join the biotech club, look for internships/fellowships or consult for a company. Also, don't be shy about emailing and networking. Often times, opportunities arise without ever being advertised so having a strong network is helpful. - Linda Vo, TRV

Biotech VC is a cottage industry with overall slow turnover. With the small number of jobs that become available each year and growing interest, it is becoming harder for advanced degree candidates fresh out of academia to stand out. My advice is to start exploring this career path early, map out the stage & models within the ecosystem you are interest in, and to leverage the now robust fellowship opportunities available to get a foot in the door. Working with people is your best chance to land a job. - Maurizio Fazio, Atlas

Talk to as many people as you can and start <u>now</u>. Many people are more generous with their time than you might think. Keep your audience wide, there are many entrepreneurial academics, founders, people in business development that might be able to provide a different perspective of what venture is. Try to end every conversation with a lead for the next conversation. Not everyone will offer to connect you with someone new but even the few that do might open new doors. VC fellowships can be a good entry point into venture if you can spare the time so be on the lookout for those opportunities. **- Nil Gural, Polaris**

I would recommend that you stay true to your authentic self, as these characteristics can be used to your advantage, i.e. communication skills, critical thinking skills, and strong analytical skills as it relates to a good business sense. The key to this job is that you must stay quick on your feet, organized, and always on the hunt. Bring the best catch back to the pack, don't bring sticks and bones. - Noelle Hutchins, Omega Funds

Offer to introduce investors to companies, scientists, future founders, or generally great people that haven't already met. From my perspective, this is a better way to get your foot in the door than sending your CV or even a warm introduction. We have also found and hired investors all over the world through their writing. - Pablo Lubroth, Hummingbird

My key piece of advice is to create your own path, don't try to mimic others. Stay curious. Form independent opinions about science, technology, and companies. Stress-test and argue with other smart people about your thinking. Talk to founders. Work with founders. Publish cool stuff (e.g. academic papers, blog posts, tweets, etc). Build a network and reputation for doing good work. Then when you talk to VCs about things that excite you, it will be clear that you're already all-in. - Patrick Lundgren, Hummingbird

My two pieces of advice are knock on as many doors as you can find, and do your best to stay positive when invariably not all of them open. No one can tell you how long and winding that road will be. As far as I can tell, the only things you can control are how prepared you are when you do approach a door to knock on it, and how you feel after the process has gone positively/negatively/anything in between. - Roman Camarda, Novo Holdings US

To kick things off, it's a smart move to broaden your knowledge horizon. Dive into different subjects beyond your usual expertise and keep up with what's happening in various fields. Then, it's all about making connections. Reach out to your alumni network, try some cold outreach (just make sure to find common ground), and hit up those investor-friendly conferences to build your network. Once you've got those connections brewing, aim for a VC internship to get your foot in the door. From there, subsequently make your way into venture.

- Sahil Chopra, Vertex Ventures HC

No given candidate is the right fit for every venture firm - and to be the right fit for a firm you often need to bring specific knowledge, relationships, or traits that will make the firm stronger as a whole. I advise folks considering VC to get exceptionally deep in 2-3 areas of interest. Not only will this show you can add unique value to a firm, but it shows you're capable of getting yourself to a deep level of understanding, a process that will need to be repeated across different areas. - Shoman Kasbekar, Foresite

Internships/fellowships are definitely a great way to gain exposure and build network within the biotech VC community. Beyond that, there are a lot of great books, podcasts, and online publications continue learning the business! - Suan Tuang, TCGX

To find a job in VC, I typically encourage people to do one or more venture fellowships to gain exposure and experience in venture capital. While I didn't take this path, these roles can often translate directly into full-time roles or set you up to find one. Don't hesitate to reach out to people at various levels as part of your search. People are usually happy to chat and jobs are

often out there but not posted. The biotech VC community is small – so the more people you know, the more likely you are to hear about an upcoming role.

To excel in a job in VC, I would strongly encourage people to be present in the classroom, lab, and/or clinic. If you have already decided to become a VC, perhaps especially so, don't lose sight of becoming a world-class physician or scientist - you only get one chance to train and investment in this phase of the journey will yield enormous returns once you are in an investing role. How you do anything is how you everything, so bring your absolute best to the experiments or patients in front of you. Your ability to make an impact on diligence calls and in board meetings is strongly related to the core skills, knowledge and habits you cultivate as a trainee. - **Travis Hughes. Digitalis**

7. Advice to prospective or first-time entrepreneurs in 2024, as they bravely pitch to VCs in the new year?

Articulating a clear view on where this approach sits in the emerging competitive landscape, how the proposed financing will unlock key value creating catalysts for 1-2 programs, and why there is favorable risk / reward for a new investor can help a company stand out right now. - **Alex Loftis, Vida**

Talk with investors early – well before you've done any formal pitching. Most investors are happy to be a sounding board. **- Alim Ladha, MPM**

Take time to understand your audience (VCs) and communicate your pitch accordingly. It pays (pun intended?) to understand what governs the drug development industry. Many life science entrepreneurs come from academia, an ecosystem in which incentives will favor pursuit of novelty for the sake of knowledge advancement and scholarly discourse. While drug development certainly also rewards innovation, there are several other considerations for developing a new drug. Non-exhaustively: a new drug should serve an unmet need, be efficacious, be safe, be manufactured reproducibly, be produced/sold/reimbursed in a way that allows profit, address a patient population that is identifiable and understood, etc. There are risks associated with all the above, and the job of a VC is to understand the opportunities and risks associated with investing in a company, while also balancing their portfolio. Understanding this vantage point will help you tailor your pitch. - Amanda Chen, Vertex Ventures HC

The last couple of years have not been easy for entrepreneurs. Clearly articulating the "why now?", your technology's differentiation, and the bar for success in your field is important as ever. In the current environment, ensure that the financing plan efficiently drives to the next major value-creation milestone for your company. If a platform, clarity and discipline on defining the 1-2 key products/applications for the technology – that create value in themselves, and also de-risk the underlying technology – are particularly important right now. Finally, it's never too early to build relationships with early-stage investors and gather feedback whenever possible. - **Aniga Tasnim, 5AM Ventures**

If you get asked a question you don't have an answer for, don't try to talk your way in circles around it, unless you can of course think of something credible on the spot! VCs take a ton of pitches on a monthly basis, so there's a built-up pattern recognition when it's likely evident when the answer clearly isn't there. You'll likely get a lot of no's from VCs when fundraising — expected, and definitely normal — try your best to understand the true specifics of why the group is passing, so you can work towards solving for this, especially if it's a data / experimental related issue. - Artie Arumov, Qiming

It all comes down to effective storytelling – who are the cast of characters, what is the conflict, what is the resolution, and how do you get there? For biotech startups, telling the story in a clear and crisp, data-supported way is the best way to capture attention and get investors to understand what exactly you're building. It's worth remembering that investors have dozens of companies competing for their attention at any given time. Therefore, the extent to which you can compellingly answer both "why" and "why now" in a logical way, often determines whether your company gains traction internally at a given firm. To be clear, by storytelling, I don't mean overzealous "spin" or "selling" which can come across as either disingenuous or naïve. Rather, it is always impressive when entrepreneurs are clear-eyed, pragmatic, and upfront about challenges that lay ahead or limitations of the data in hand. Building trust is such a critical commodity for company builders and forms an important part of the investment thesis with respect to the team. - Harry Won, OUP

The market for biotech and therapeutic investing is accelerating in 2024. We're not out of the woods yet concerning the 2022 market downturn. However, the future for the industry looks bright as investors have strong levels of dry powder to deploy, and great founders and technologies are seeking syndicated funding opportunities. Founders that pitch must be lean: present articulate development plans that push toward clinical value inflection points as fast as possible. Also, be aware that efforts to syndicate can take months to assemble investors, so don't expect the process to happen quickly. **- Danjuma Quarless, Abbvie Ventures**

We work in a very collaborative industry so if a VC passes on your financing don't be afraid to ask them for introductions to other funds. There's a high likelihood they'll know a few people who could be a better fit for the stage or area that you're working in. - James Buxton, NEA

In therapeutics, 2024 feels like a year where biotech markets are finally returning to a place where good data is rewarded, and non-validated targets are attractive again. That said, timeline to data is important, and investors want to see efficacy not just safety to want to take a big bet into new modalities. - Jason Wang, Frazier Life Sciences

Focus on the "why" first – why is your work important for patients, and what unmet need are you addressing? Additionally, I recommend always seeking feedback, both positive and negative. It can be helpful to understand why investors were unable to get across the finish line, both to improve messaging but also to inform company strategy and tactics. Investors who pass on the

current round may ultimately become shareholders and valuable thought partners a few years later. - Kevin Li, Frazier Life Sciences

The first time you meet a VC should never be a pitch. For prospective entrepreneurs, this means that you should be spending a significant amount of time trying to meet investors and learn about them and their interests. Cold intros are generally very low yield, so build slowly from your existing network (e.g., your academic network) asking for 1-2 warm intros. This is not a sprint but a marathon. Set clear and actionable goals for yourself on building out your network, whether that be attending X networking events per month, new coffee chats, or even spending a certain number of hours engaging with your school's tech transfer group. When I was at Chicago, I had a completely maniacal Excel sheet where I had mapped the top 100 healthcare funds across the Penn and Chicago alumni networks, my LinkedIn network, and then mapped out key "nodes" of secondary connections that I realized would unlock a ton of value. I'm not sure I would recommend this approach for everyone, but take building and maintaining relationships seriously. When you finally get to a pitch, it's such a relief to see a friendly face and often that's the person who can intro you to the rest of their group as someone that they know and respect. - Lauren Mifflin, Frazier Life Sciences

Can't stress this enough: Articulate clearly your target & product thesis A second point, in your early VC interactions ask for help and feedback to navigate the landscape of likely investor fit for your project. Lastly, remember that rejection is often about the idea/project, but just as often about fit/externalities (Fund cycle, portfolio strategy, timing etc.) - Maurizio Fazio, Atlas

A good first pitch is meaningful – prepare well, ask "friendly" investors to give you feedback before you get on the road, make sure you are delivering a crisp and clear message, take the time to cater your pitch to your audience Today, more than ever, efficient use of capital matters – make sure that you have a solid development plan and the capital you are asking for can take you to meaningful milestones Be resilient - there may be many "no"s along the way but you are your best advocate and all you need is a few "yes"s - Nil Gural, Polaris

Align yourself with the right people and get feedback early on your pitch. You may have to go through multiple iterations, and the overall fundraising process isn't for the faint at heart. I also think that the older biotech veterans also need to show the younger founders the ropes and be willing to mentor and pass the torch. - Noelle Hutchins, Omega Funds

Don't appease investors to the point of sacrificing your vision. As my team often says, investors have many opinions, but they won't suffer the consequences of a poor decision in the same way a founder will. So don't implement advice that you believe is not in the company's best interest because your investors suggest it or because you think it will be more likely to get financing from them on the next round. - Pablo Lubroth, Hummingbird

When preparing a pitch, constantly ask yourself "so, what?" I think one of the hardest parts of putting together a pitch is ignoring the impulse to share everything you think is important and

instead just focusing on the most important parts of the story. A pitch (if it goes well!) is just the start of a relationship and just the start of the diligence process. So, rather than trying to cram every aspect of a story, every possible direction for the technology, and every piece of data into that first presentation, I'd encourage first-time entrepreneurs to try to refine their story to only what is most essential (and why it's essential) and to put the bottom line at the top in plain English. Prospective or first-time entrepreneurs (or really anyone interested in biotech) can find more advice and resources on RA University and Gateway. Also, we publish cool stuff on RApport, like comprehensive analyses of trends in the biotech public markets and a video where I talk about psychedelics. - Rebecca Silberman, RA Capital

There has never been a better time to be in biotech. I couldn't be happier doing what I'm doing. My advice would be to give a pitch that you couldn't be happier giving. - Roman Camarda, Novo Holdings US

Highlight the significance of milestones and how they contribute to value creation, backed by concrete examples. Secondly, devise a realistic budget and timeline that instills confidence in stakeholders. Lastly, have a slide summarizing the main points of your presentation to ensure investors understand the key takeaways along with the big picture.

- Sahil Chopra, Vertex Ventures HC

Milestones, milestones, milestones. Exactly what will you accomplish with the capital, how can we be confident you will accomplish these milestones, and why will these accomplishments drive a value inflection for your company? We're in an environment that highly scrutinizes fundamentals. While storytelling remains as key as ever, also drawing a logical bridge to derisking milestones is critical. - **Shoman Kasbekar, Foresite**

Continuously refine your pitch and actively seek feedback from trusted advisors. Ensure you articulate your unique differentiators clearly. **- Suan Tuang, TCGX**

Refine your story before you start pitching to VCs. Flex your network and get honest and critical feedback from trusted advisors. VCs talk to each other, so make sure your story is prime-time ready before you start fundraising. Don't get discouraged when you hear no because you will almost certainly hear no more than yes. No is a two-letter word, but no two no's are identical. People say no for a vast number of reasons – many of which have little to do with your story (e.g. goodness of fit, fund dynamics, stage of focus, portfolio strategy, modality/TA). Ask for feedback, but don't take it personally when you don't get as much as you feel you deserve. I strive to provide useful feedback that genuinely reflects my thought process, but this takes up a lot of time and is hard to maintain across all the companies that I interact with. Finally, be patient and kind to yourself. - Travis Hughes, Digitalis

8. Any predictions for what biotech will look like at the end of 2024?

There's certainly optimism for additional strong IPOs and M&A activity in 2024. As pharmas continue to look for assets to off-set LOE-related revenue cliffs, I imagine you will continue to see acquisition and partnering of de-risked modalities and / or interest in late clinical-stage assets. - Alex Loftis, Vida

When thinking about market forecasts and their validity, I like to read the opening of Howard Marks' 2008 memo. A relevant excerpt: This is a great time for my favorite quote from John Kenneth Galbraith: "There are two kinds of forecasters: those who don't know, and those who don't know they don't know." No one knows about the future, and that's more true now than ever . . . literally. I am certain that science relevant to therapeutics is humming along – likely faster than ever – with exciting discoveries and progress happening constantly. On the backdrop of vast unmet medical needs and rising costs for medical care, it's a great time to be in biotech. - Alim Ladha, MPM

The biotech capital market is coming back, both in sentiment and numbers. In 2023, only about 25% of capital raises were announced without a clinical/regulatory catalysts driving the financing. So far in 2024, 40%+ of deals have been "opportunistic" – i.e. lacking a driving catalyst (Jack Bannister, Leerink). Funds have dry powder to deploy, and have been more proactive in driving deals than they were last year. On M&A - as several pharma groups continue to plug revenue gaps from impending patent expirations, we might continue to expect a focus on late clinical- / commercial-stage M&A for a bit. However, we should soon be able to expect a shift back toward earlier-stage deals as pharma also look to technologies/platforms that will fuel growth for the next decade – both through large-scale M&A and risk-sharing partnerships – leaving new biotechs that are strategic about building business development engines in their pipelines well-poised to transact. - **Aniqa Tasnim, 5AM Ventures**

I think precision oncology will return into the biotech spotlight, catalyzed by promising clinical readouts within emerging target classes and with novel drug modalities finally making value-accretive pushes! We'll see investments and data readouts for therapies against novel targets, and learnings from the last ~4 years of antibody and cell therapy technology will finally begin to show themselves with exciting opportunities both entering and reading out in the clinic. The current sentiment is incredibly asset focused (show me a DC through clinical asset) and these are certainly getting financed – by the end of 2024 I think we'll see an increase in more Seed investments, as the bullpen of high-value asset investments begins to empty out. - Artie Arumov, Qiming

As I mentioned, the biotech sector is shaping up for a strong 2024 if the first two months are any indicator. The XBI crossed over \$100 for the first time in two years—this isn't definitive data that we're in the clear regarding IPOs and strong pharma M&A opportunities. However, I feel positive that we're trending in the right direction, both in terms of early-stage investing (seed, Series A, new company creation) and late-stage investing (Series B, PIPEs, IPO, and M&A). - **Danjuma Quarless, Abbvie Ventures**

The JPM conference is a great place to take a pulse check of the industry and the general tone this year was generally one of hopeful optimism. A lot of this was buoyed by increased M&A activity; this combined with the reality that VCs will need to start deploying the dry powder they have been sitting on perhaps signals reasons to be hopeful that we'll start to see more deals get done in biotech. These themes and more described in greater detail from a great <u>JPM recap</u> from Aimee Raleigh at Atlas Venture. - Harry Won, OUP

While the PIPE activity in the public markets is certainly a recent positive trend the uncertainty surrounding what the Fed will do with rates in subsequent months and the upcoming US election doesn't fill me with hope for the number of IPOs in the second half of the year. History tells us that M&A activity drops up in the months ahead of an election and I don't see why that shouldn't be the case this cycle. Finally, the XBI has been so tightly and inversely correlated with interest rates that we should expect to see private deal activity roughly follow activity in the public markets, all be it a few months behind. - James Buxton, NEA

The IPO window is already opening but mostly reserved for companies that are 6-9 months from proof of concept data or late stage clinical data. That likely will persist for 2024. M&A will continue to be strong, but follow a similar pattern for near term revenue products, compared to bolt on technologies that pharma will invest internally on. Products rather than platforms will therefore dominate M&A headlines for 2024. - Jason Wang, Frazier Life Sciences

Our sector is inherently volatile, but good science and good data that has the potential to meaningfully improve patient care will always be rewarded, regardless of the macro. I am also hopeful that we will continue to make progress in neurodegenerative disease, an area with relatively fewer wins relative to others. **- Kevin Li, Frazier Life Sciences**

So far the start of 2024 has been encouraging on the M&A and IPO front, which I think will continue to stay more favorable than the majority of 2023. I hope that we as an industry will retain the discipline in financing companies to value inflection milestones rather than reverting back to the 2021 norm of raising as much money as you can to start as many different programs as you can. In that spirit, I think early stage funds will continue to focus attention on clinical stage companies over the course of 2024. That said, there is a ton of dry powder that company creation firms have raised or are currently raising across established groups (e.g., Flagship, ARCH) and newer entrants (e.g., TCG Labs, Scion Life Sciences), so suspect we'll start to see a good amount of early building as well. - Lauren Mifflin, Frazier Life Sciences

I certainly hope for continued positive momentum and for the market greenshot to take root – **Maurizio Fazio, Atlas**

Hard to predict but I expect the positive trajectory to continue with M&A and IPO activity picking up; albeit slowly. It is more important than ever for companies to be thoughtful about important milestones, capital efficiency and ruthless prioritization. - **Nil Gural, Polaris**

We will continue to see M&As in biotech for differentiated clinical stage products, not necessarily confined to one modality and/or target indication (but have seen a lot of ADC and radiopharm deals for Oncology and metabolic deals for obesity). In a down market, there will always be opportunities for company creation and venture investing. The key is looking towards the horizon to understand the greatest problems in drug discovery and development to address diseases with high unmet need. **- Noelle Hutchins, Omega Funds**

I'll give another tip of the cap to Howards Marks, who says you either think you know, or you think you don't know. I don't know what the end of 2024 will look like, but I do know that thus far in 2024 I've seen numerous exceptional investment opportunities, and I couldn't be more excited to take part in what I perceive to be a thriving ecosystem. - Roman Camarda, Novo Holdings US

After a very upbeat start to 2024, I foresee the biotech markets ending the year on a rather volatile note, especially with it being an election year. We can expect ongoing M&A or dealmaking frenzy among major pharmaceutical players, particularly in hot sectors such as cardiometabolic diseases and antibody drug conjugates/radiopharma in oncology. Additionally, I anticipate significant consolidation within crowded fields like cell and gene therapy. Biotech companies that prioritize strong science, data, and have the potential to improve patient care are best positioned to make a lasting impact, regardless of market fluctuations.

- Sahil Chopra, Vertex Ventures HC

Starting at JPM this year, much of the uncertainty and anxiety of the past year has given way to a cautious optimism if not excitement. As I write this, the XBI turn-around appears to be well underway along with a re-opening of the IPO window. Despite an uptick in deal flow and numerous green shoots, I think investors are still approaching new opportunities with the increased scrutiny of the past year. Biotech investors are looking to reward high-quality clinical data (Series B+), while looking for promising new opportunities for early-stage investments (Seed/Series A). However, this leaves many great companies stuck somewhere in the middle. The biggest challenge of 2024 will be the pre-clinical Series B, as companies and investors alike search for ways to attract outside investors to transition promising programs into the clinic. - Travis Hughes, Digitalis