LIFE SCIENCES SNAPSHOT

A Quarterly Report on Financing Trends

THE YEAR IN REVIEW AND SPOTLIGHT ON AI
Q1 2021

orrick

Data provided by

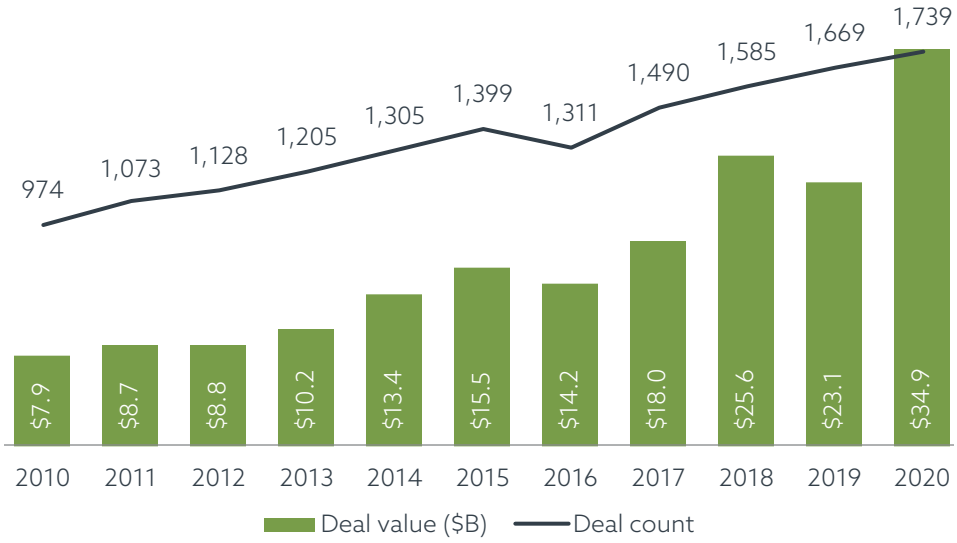
PitchBook

Key Takeaways

This edition of Orrick's series of life sciences publications reviews full-year 2020 data in depth to identify and summarize the key trends that shaped venture investment across the sector. 2020 was a banner period for many metrics, including:

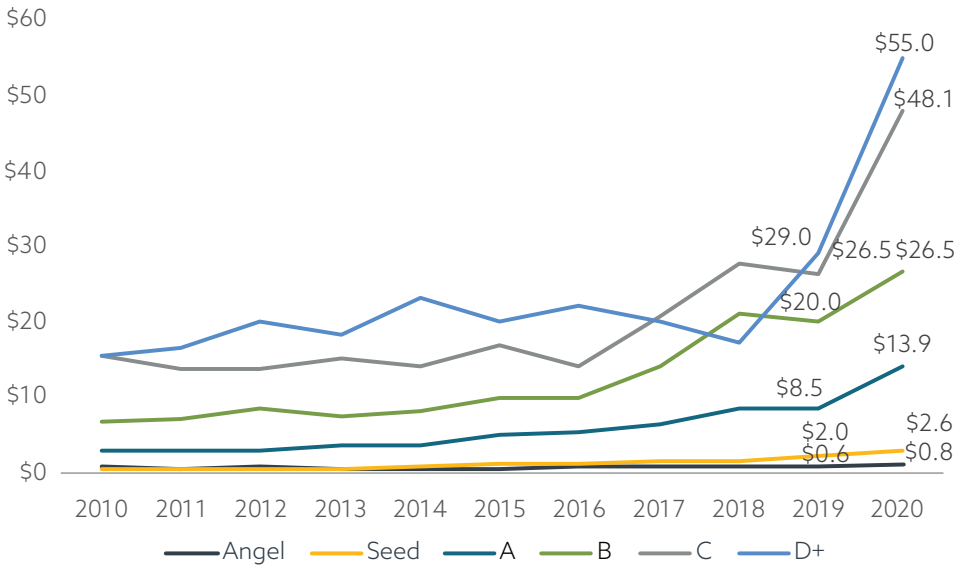
- Total life sciences VC deal value hit a record $34.9 billion in the US, far outstripping the prior high of $25.6 billion recorded in 2018, a clear indication of accelerated interest in the sector and new entrants in the space.
- Although Q4 did not surpass the record sum of capital invested in Q3 2020, it still hit the second-highest mark yet at $8.7 billion.
- Median pre-money valuations at both the early and late stages hit new highs, at $30.0 million and $70.0 million, respectively, for the year.
- In 2020, angel-stage deals represented their highest proportion of total life sciences VC deal count, signifying renewed interest in innovations that are likely in part attributable to the sheer volume of attention and capital centered around all aspects of the COVID-19 pandemic.
- Even without taking into account completed special purpose acquisition company (SPAC) activity, exits hit a record high of well over $50 billion in value in 2020, eclipsing any prior annual total.

Life sciences VC deal activity



Source: PitchBook | Geography: US

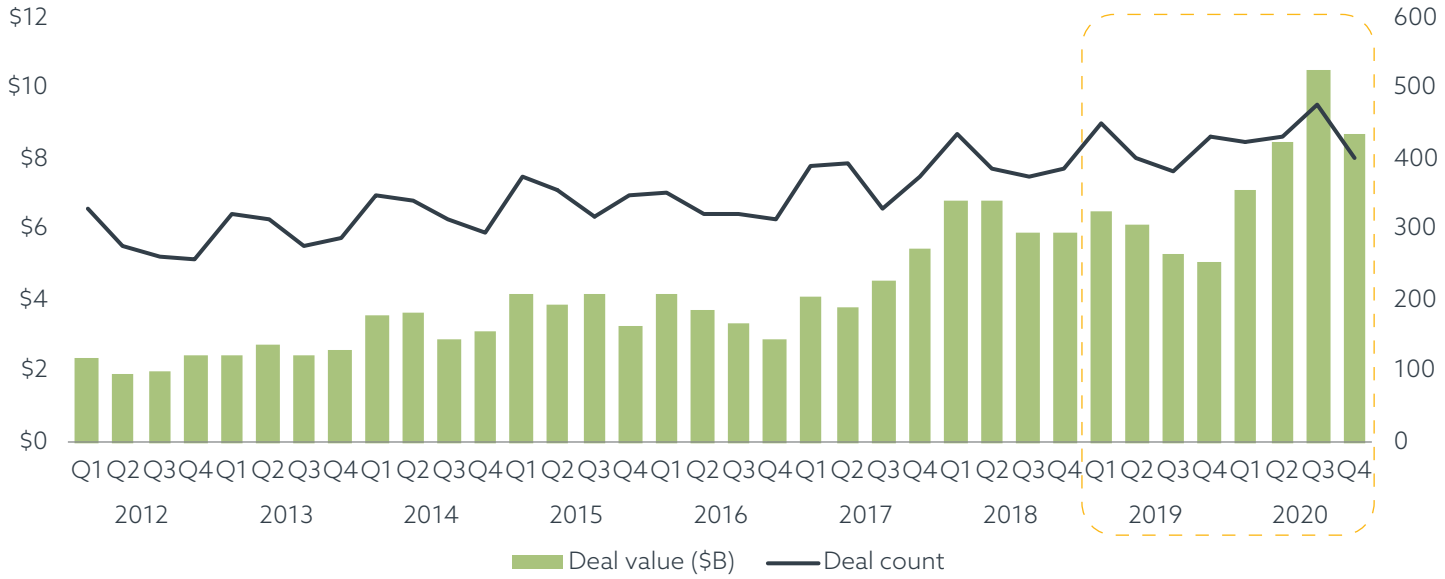
Median life sciences VC deal size by series



Source: PitchBook | Geography: US

Market Analysis

Life sciences VC deal activity by quarter



Source: PitchBook | Geography: US

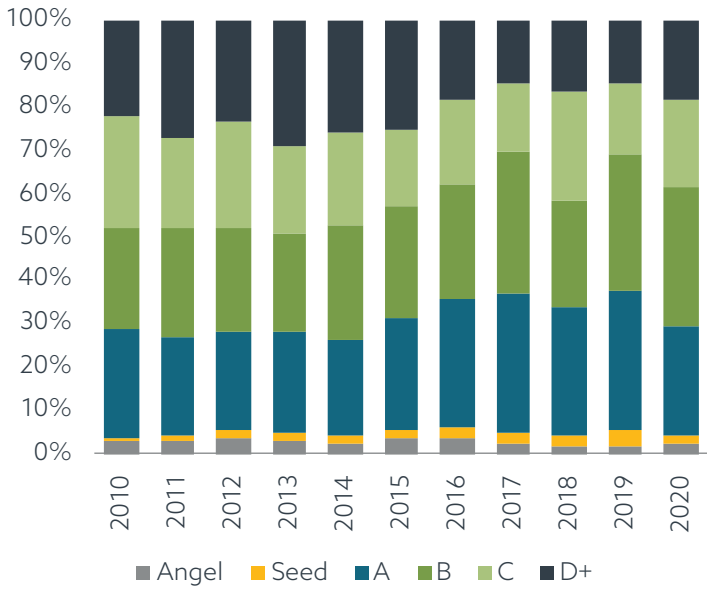
Few sectors were as directly affected by the COVID-19 pandemic as life sciences, with potentially long-term implications emerging. While other industries experienced accelerated growth or significant challenges, the life sciences sector experienced both. Clinical trials grew logistically complicated, supply shortages emerged, and companies have had to re-think laboratory and working arrangements. At the same time, there has been an invigoration of research activity in vaccines and COVID-19 therapies, along with continued investment in more traditionally funded subsectors.

While COVID-19's spotlight was remarkably powerful, a redoubling of interest within the life sciences space, prompted by multiple successful exits, had already begun to encourage steady and increasingly significant VC investment activity. The fruits of technical advances—genome sequencing, CRISPR-Cas9, biologics, cell therapy, mRNA-based vaccines, AI-powered testing, immunotherapies, and so on—increasingly resulted in numerous companies advancing more quickly through the typical life sciences lifecycle. This acceleration of development underpinned a steady rate of growth in venture deal count, with scarcely a dip year over year throughout the 2010s, across all stages. Moreover, increasing sums flowed to every venture series across the sector, with the seed stage alone surpassing $750 million in deal value in 2020. A diverse distribution of capital across all venture stages is an important indicator of burgeoning interest in any sector, as it signifies that mature companies are able to keep amassing the sums needed to scale and realize full commercialization potential, and that plenty of fledgling enterprises are attracting the sums required to continue along the same trajectory. By that measure, life sciences is experiencing very promising trends in venture investment.

These trends seem likely to sustain momentum. Perhaps most importantly, the new ground broken regarding regulatory adaptability to the pressures wrought by COVID-19 could lead to more expeditious if not more lenient regulatory checklists for clinical trials. Much attention has been paid to the risks inherent in areas such as the gene editing of humans or livestock or other modifications of living organisms that may have significant commercial impacts on the modern world. However, 2020 has perhaps shone a more welcome light on some of the lesser-known issues that could benefit from reconsideration of current regulations, such as test kit validations and simultaneous clinical phases.

All in all, despite the hurdles introduced by the pandemic, venture investment trends signal record investor interest in 2021 as well as a surge of innovation and potential targets to meet that demand.

Life sciences VC deals ($) by series



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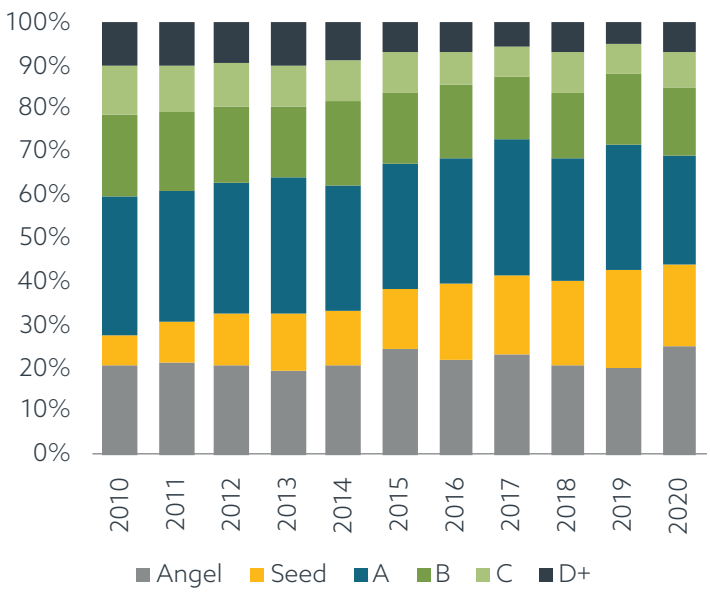
Life sciences VC deals (#) by series



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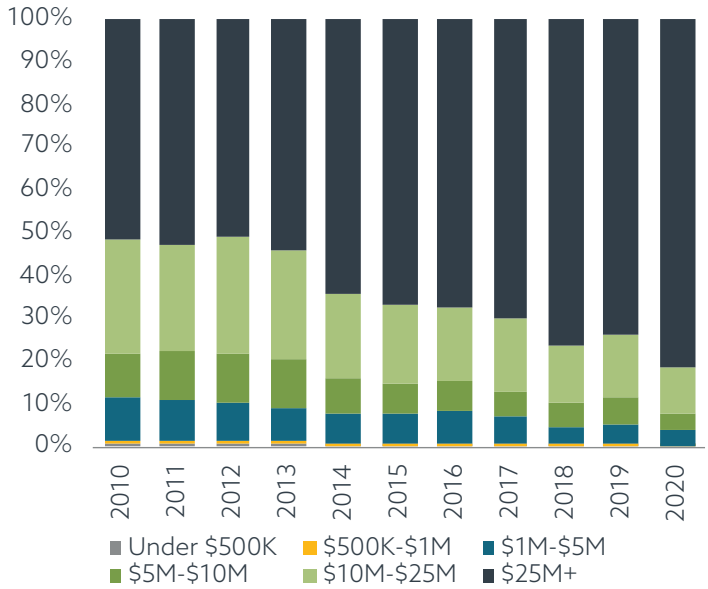
Life sciences VC deals ($) by size



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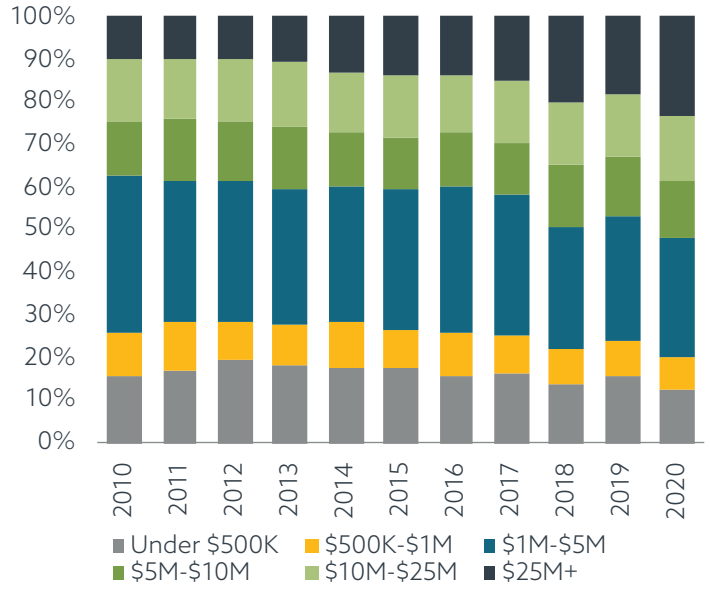
Life sciences VC deals (#) by size



Source: PitchBook | Geography: US

Roundtable

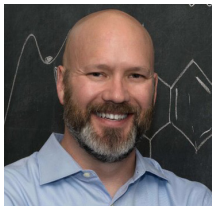
Neel Lilani: What are the key impacts that AI will have on the life science sector in the next five years? Ten years? Beyond?

Brandon Allgood: I think the target ID and drug discovery spaces will see a large impact, and we are starting to see that in the data sets. Emerging data sets and modeling allow us to characterize patients, patients' sub-populations, and molecular properties, both in vitro and in vivo. We can use this data in both the discovery of new targets for therapies and the development of more-personalized medicine. Additionally, you'll see a decrease in animal models, which, at their best, are marginally good. However, we're starting to build AI models of animals and humans and set new gold standards for testing drugs. The clinical side will take longer due to human safety concerns, and the FDA has recently put out a brief on its initial thinking around AI. It will be slower, but we are already seeing additional advancements to synthetic clinical trials, as well as the use of machine learning and AI models to design trials. In the commercial realm, we're seeing the use of real-world evidence to treat disease. We're starting to develop cures and preventative measures through AI applied to imaging and general care. There is a lot coming down the pipe in five to 10 years.

Vangelis Vergetis: Another important impact of AI can be in reversing the downward trend of R&D productivity in the industry. If I were to push Brandon's very good point above, perhaps there will be a world 10 years from now in which companies in the industry will not use animal models at all. AI can help accurately assess, speed up, and reduce risk of clinical trials

Panel

Contributors



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Separately, I would also like to mention other treatments that are beyond making drugs. For example, there are companies out there that develop video games as a form of therapy to treat, say, ADHD, substance abuse, or other conditions. Digital therapeutics and software, among other things, are starting to become more prominent. The AI bit is that these platforms learn from the user and continue to improve and tailor themselves for the individual patient. My patient experience will differ from anyone else's, and software can uniquely deliver a truly personalized therapeutic to different patients.

Finally, a broader but also related point to make here: In my view, the rate-limiting factors for all these step changes to occur are less about the AI algorithms themselves, and more to do with the overall culture around adoption of AI, regulatory issues, and data availability.

Angeli Moeller: When it comes to impact, we have to ask ourselves, "What do these AI advances mean for doctors and patients?" Roche has an exciting pipeline right now, and that's due in part to an increased investment in data, data cleaning,

and building a community of highly skilled data science talent. Beyond the pharmaceutical industry, AI is poised to have a significant impact thanks to the data sets produced by continuous remote monitoring. As patients continue to receive care at home during the COVID-19 lockdown, we see solutions that combine at-home treatments with alerts sent to healthcare professionals for timely interventions. Now, more than ever, we see machine learning and predictive analytics free up capacity in the healthcare system. That's where the societal impact will be highest. The hurdle will be ensuring investment in access so that these solutions are not just available for the few, but for the many. This care must be accessible to as many people as possible.

Andrew Toy: I've been in the enterprise industry for a long time, and I have found this to be entirely systemic. Once I was talking to a large fast-food chain and said that we could do model training to optimize drive-throughs and the customer experience. Their top priority was, "How can we change our menus from paper to TV screens?" Not an AI menu. Not a dynamic menu. That is what it's like in healthcare right now. It's not an R&D issue. Here's how I explain the most basic ML models: Imagine you had 1 million additional radiologists just standing there. If you don't know what to do with them then you don't have a modeling problem. But if you do have tasks for then, then great! This is what ML models can accomplish. Clover is very focused on the accessibility of primary care physicians. If we can help them do their job better by adding a model, we will objectively offer improved care that is more beneficial for us all.

Gregg Griner: Our clients spend a great deal of money and, maybe more importantly, a significant amount of time on preclinical and clinical studies. In many cases the design of these studies is dictated by scientific principles and FDA guidelines that are decades old—ancient history. With the science and innovation having advanced far beyond these principles and guidelines, particularly with the rise of AI and "organ-on-a-chip" technologies, how difficult do you think it will be to get the FDA comfortable with these new technologies and accept them in lieu of traditional animal studies?

Brandon: I don't see us getting rid of animal studies all at once. I see us moving to all tests being confirmatory of prediction. I think we'll see a large reduction of animal testing and more straightforward confirmatory tests. On the clinical side, FDA evaluators need to see the proof, likely through getting the software and making predictions for themselves to build up confidence. First, they will need to get models that are good enough. But to have better predictions, we need greater quantities of better, more representative human data. To Angeli's point, human data needs to improve, and we need to improve our collection. Not only that, human data takes time to generate. You can't go back in time. One of the limiting factors is that you must set-up the collection system, and then you must wait for the data to come in. Additionally, there is the matter of explainable AI and the need for improvements there. Pre-clinically, you can have black boxes, but as you move into the clinic with humans, the models need to be explainable to an average doctor and have error bounds.

Angeli: We are all working toward the common purpose of ensuring a treatment is safe when the patient gets it. New technologies such as AI will be more rapidly adopted in areas where they work in the patient's favor as, for instance, when we use predictive analytics for rare diseases when patient numbers are low. The regulators just want what's best for the patients, and this is a fantastic opportunity for the industry to demonstrate those benefits.

Neel: How is AI transforming patient diagnosis and treatment apart from image recognition? Is this particularly applicable to telemedicine? How do we use AI to enhance remote patient care and continuous remote monitoring, diagnosis, and treatment?

Andrew: I will say that I am very bearish on the use of telemedicine and report monitoring, but I am very bullish on the concept. The ability to drive compliance on devices is very low. Use the device incorrectly or irregularly and your data is tainted. If you give a patient a health-monitoring watch, even for free, they won't use it. They will forget to charge it, and you get no signal for days. However, when we have passive monitoring, of which I'm a fan, we will see much better data. Would you like to see your doctor? We can offer you WhatsApp video. Would you like to put this monitoring device in your home? Yes. When do you offer continuous monitoring? Would you like to be monitored all the time? The answer is no. This panel is full of Type-A personalities who would love that, but we are not the majority of the population. There are patients who say, "I worry whenever I get my cancer test done." But the test is confirmatory in nature, and the result is the result. They would rather not know the result so they can sleep at night. It's very human.

Neel: How will AI play a role in healthcare ethics? For example, will AI select how to allocate limited medical supplies based on the likelihood of a successful outcome?

Vangelis: There would be more personalization of medical care if AI is used correctly, and that can be very positive. On the ethics side, there are some things we know fairly well how to do, for example avoiding biased models, even though there is still much more to do there. Will we ever be fully aware of unintended consequences? We don't know as much about that. If we talk about therapeutics, for example, the analogy in my mind is to think about the side effect of a drug we didn't see because—for example—our clinical trials were not large enough. The same concept should apply in AI, and we still need to be open to the possibility that some of those "bad" things will happen. We do our best

through clinical trials to make sure that drugs will not kill patients, but sometimes they unfortunately do. Similarly, AI will make mistakes, and we should accept that. We of course need to have a high bar, understand why those mistakes happen, and try to avoid them, but our bar should be no higher just because one random thing happened, or just because the mistake was made by a computer rather than a human.

Andrew: This makes me think of self-driving cars. If a self-driving car makes a bad decision, everyone will report on it. But we won't report on how many people have been saved or how many have died driving their own car.

Brandon: You have to also think about psychology. People are used to interacting with logical machines, not statistical machines. My favorite example is to imagine a statistical ATM. With a logical ATM you put your card in, you type in $100 and you get $100 out of your account. If it were a statistical ATM you might get $100; you might get $80 or $120. In the latter cases is the ATM broken? If you only have one or a few samples from a statistical machine you cannot conclude that it is broken, but if you are used to logical machines you will likely forget this and conclude that it is broken. AI is a statistical machine. It's a thing we need to adjust ourselves to. And regarding Andrew's and Vangelis' comments, AI did not create bias in our medical system; it already exists. The vast majority of available human data is from predominantly wealthy areas, and these are not exactly the most diverse populations. We need to focus on diverse data collection. In the meantime, we need to reweight the existing data sets we use in our models to reduce the bias. AI has the potential to make bias 1,000 times worse, and it's on us to make sure that doesn't happen.

Angeli: The charity Rare-X, of which I am a board member, recently launched a diversity and inclusion project co-funded by several industry partners to ensure the datasets they collect reflect diverse populations. One of the issues they are exploring is how we ask questions when data is collected and how we build an awareness that stigma attached to specific diagnoses may affect the responses received from patients or caregivers. Aside from hidden bias in datasets, another challenge in implementing AI at scale is the development of the skilled workforce needed to develop and work with AI solutions. I am very interested in university programs that couple data science courses with ethics and healthcare.

Neel: Let's talk about patient data. Will AI allow healthcare to be truly portable? Will there be a master record that intelligently tags data to one patient from disparate sources and develops a holistic view of individual health?

Andrew: What is the impact of model training? We need to update the guidance so that it will be very powerful. As a technologist, I know model weights back into patient health information. We could be entering a new era where model portability revolves around model training. We can exchange models internationally. We are not very different since we are all humans, but those differences can be informative. We have a lot of cases of diabetes in the US but not very many in Asia. That model can be sent over to Asia, and they can send us a model for hepatitis, which is very common in Asia but less common in the states. We can never share patient data, but we can share models and more in the future.

Angeli: It is important to validate AI models on data sets from different sources. Such validation makes it possible to provide AI-solutions to different populations globally. As a global organization, we work with partners who cannot openly share datasets, and in such cases federated learning is proving to be an emerging solution to this challenge. The model moves from data set to data set, but the data itself does not move. However, one challenge is that everyone must agree to the same data standard, which ties back to Neel's question on data tagging. This is what is holding us back on scale right now. We will have to all agree how we are going to internationally standardize healthcare data sets.

Vangelis: Part of the assumption here is that patient data exists in each country and that it's clean and connected. In reality, however, my personal health data is all over the place—across different insurance companies, hospitals, and pharmacy benefit managers in the US. Some of my data is in other countries. How do we get all that in one place? How do we connect all these pieces of data and consolidate it? If we solve these questions, we can do all sorts of wonderful things. Israel provides a good example of how to manage data, and other countries have streamlined the process as well. In short, my view is that getting the right data is the main obstacle to using AI in healthcare. We're all machine learning specialists here, and I would say that getting the data is 80%–90% of the work.

Brandon: I also agree with an earlier comment that HIPAA needs to be updated to a modern standard of privacy and access, but there are also other barriers. In the Western world, we have a common set of disease labels. But in many parts of Asia, for example, they think about disease phenotypes in a different way and will often use very different labels. In addition, modern Western labels are based on phenotypes with many underlying molecule dysfunctions leading to the same label. I would love to see a universal standard, but we need to develop disease labels that better reflect the disease. If you have Alzheimer's disease, what stage is it in? If you have a glioma, where is it located? These things matter a ton. Currently, 95% of data science is cleaning the data, and 5% is making the models. We need to move those percentages.

Neel: We need to balance the human touch and AI because medicine is an inherently personal profession. How do modern practitioners ensure their individual judgment and experience are not superseded by an algorithm?

Vangelis: Here is one example of messy human data. When NLP algorithms parse through doctor's notes, there are a lot of interesting things to potentially learn, particularly when you couple the data from those notes with medical interventions and, ultimately, patient outcomes. But some doctors write things with an eye toward getting reimbursed by the insurance company, others so that there is no legal liability, etc. And that's perfectly understandable, but the issue is that—to a machine—the notes by the doctor do not fully represent reality; therefore, AI models that are built on those notes may be inherently skewed.

Brandon: This is a problem with real-world data: What are the motivations? Doctors' notes are often not 100% truthful. They are doing things for the benefit of patients, and this doesn't always lend itself to being 100% truthful because the incentives aren't always aligned. I think we need to create models and meta-models to correct for it.

Andrew: And now you need to meta-model the doctors, and you need more data. We have had some success on outlier modeling. We discovered a nephrologist (kidney doctor) was also offering dermatology; it was an outlier, and the model did find it. We do have an ability to watch prescribing patterns, and that's the best of this right now. I want to re-emphasize the meta of this. Some doctors are coding and billing to truly have them and some are using it to make sure reimbursement occurs. There is a meta game here. Here's another example: We had a doctor ordering a colonoscopy, and he picked the code extremely quickly. Their thinking was, "I always pick this one, and this is the combination that gives me the least headaches from the billing department." Hopefully, my outlier model would notice that other doctors write different notes, and the first doctor's note should be flagged as an outliner.

Angeli: Ultimately, a healthcare professional wants to spend more time with their patient, and AI-based solutions can free up this time. They can also help doctors identify opportunities for early intervention, preventing more serious progression of a disease. If we can prevent serious acute events, such as a visit to an emergency room, through timely interventions, then we can see real impact on the cost of the healthcare system and reduce inefficiency. And we can't forget that there is always an intelligent human leveraging the AI-based solution. There is still that highly trained doctor/molecular biologist/chemist looking at the prediction and deciding how to move forward.

Brandon: I always try to reassure researchers that they're not losing their jobs. Humans are uniquely creative and have a broad set of knowledge that a narrowly trained AI model lacks. We need humans in the loop with the AI model, especially with patient care.

Vangelis: To paraphrase a quote by Derek Lowe, "It is not that AI will replace drug developers. It's that the drug developers who use AI will replace those who don't."

Andrew: We work very closely with providers. From a user experience perspective, if you show a physician that a suggestion was generated by AI, we see a lower uptake rate because it came from AI. If instead, we show how it was generated because of data points describing the purpose, then we see a significantly higher rate of uptake.

Angeli: This reminds me of when TomToms became available. Some people were very resistant to being told where to drive. We need to make sure we're asking doctors and patients, "What is going to be useful for you?" and, "What do you need?" Here is a highly skilled healthcare professional. What sort of user experience will be helpful for them and save time? They need to know what sort of data we are collecting and be able to absorb it quickly. They don't want to learn a whole new system. Whatever solutions are developed, we must make the whole patient journey as smooth as possible.