JUNE 2021

WILSON SONSINI

THE LIFE SCIENCES REPORT

Managing IP Development and Capture at a Growing MedTech Start-Up

MedTech start-ups often center around a core technology covered by the earliest company patents. As the company develops, patents are often filed for improvements and refinements to core technology and eventually for supportive technologies and even new product lines. Start-up companies frequently start with a very informal process to develop and file intellectual property. As a company grows, there starts to be a need for a formal process. In this article, Darby Chan, a senior associate in Wilson Sonsini's patents and innovations practice, surveys executives leading IP development and capture—Angela Murch at InCube Labs, Bernard Shay at Earlens, Lakshmi Mishra and Chris Flaherty at Nalu Medical, and Steven Bowers at Exo Imaging—on how they manage these processes.

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At what stage of company growth is it necessary to formalize an IP development and capture policy?

Angela: It is never too early for a minimal policy, but in a start-up environment, it realistically might be a very informal policy for quite some time. As the number of employees increases, the need for a more formalized policy may become self-evident.

Bernie: At the very initial start-up stage for any company that expects to file and rely on its patents.

Mishra & Chris: In teams that are relatively small and where the projects are known to those managing IP, new ideas can be captured in an informal manner and most aspects of a company's system can be filed on. As the team grows (>25 developers), a formal process may need to be considered.

Steven: Any company that views innovation and technology as a foundation for its long-term growth, its product or service offerings, or investor value should formalize an IP policy on Day One. This is a company culture issue that, if neglected for too long, can create long-term vulnerabilities. It begins with a recognition by company founder(s) that IP will represent some of the most valuable company assets, at least in the short term while initial research, development, and prototyping is occurring. Promoting a conscientious IP culture at the very beginning will pay dividends in terms of recognizing key IP assets, and mitigates the risk that key, foundational IP will not be recognized for the value that it conveys and not be protected in a timely manner. With just a little bit of upfront programmatic organization—that need not be overly formal or capital intensive—an early-stage company can position itself for long-term IP advantages.

What are some key programs and policies to put in place?

Angela: IP and confidentiality agreements should be in place with all employees, and there should also be IP and confidentiality sections in contracting and consulting agreements. Ownership of IP should be decided up front when dealing with third parties.

Occasional training and reminders regarding various aspects of what is confidential and how to treat confidential information are important, as is an NDA policy and related training. A policy that requires IP counsel to preview public disclosures (e.g., publications, presentations, articles, and websites) is critical, to ensure coverage by existing patent protection and to remove confidential information.

Bernie: Programs and policies should be put in place for invention disclosure submission and review, trade secret protection, and the use of confidentiality agreements.

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Mishra & Chris: An IP review at the start of development (i.e., a product clearance or freedom-to-operate study), multiple check points along the development path, and a final retrospective. Broad, multidisciplinary meetings solely for the purpose of discussing any and all ideas that might have been generated during the development process that ought to be captured in filings should be conducted. Regular IP searches that track all players in the company's field, since company inception can be important, too.

Steven: First, consider adopting a formal written company IP policy, promulgated throughout the company, that explicitly recognizes the importance and value of company IP, respects third-party IP rights, and includes explicit guidelines to prevent prejudicial risk to company IP. Push responsibility onto each individual to act responsibly and appropriately. Second, create a process of invention disclosure, including an invention disclosure form and submission process. The key is to minimize the overhead (time and effort) required by inventor(s) to complete and submit an IDF. If the process is too clunky, time consuming, or onerous, inventors will find excuses to avoid it. Third, if budget allows, consider an incentive program that awards inventors for submitting quality disclosures. It need not be lavish, but should recognize the extra time and effort that they take from their busy schedules to participate in creating IP. Finally, if the volume of submitted disclosures exceeds available resources, consider forming a review committee, comprised of key IP and technology experts, to prioritize the pipeline.

What do you think about formal, written IP and patent policies?

Angela: In the fast-paced and small community environment of an early-stage start-up, formal internal policies are difficult to enforce and may be unwelcome. Additionally, the standard policies that larger companies have adopted may not be useful in context.

Formal policies for working with outside counsel can be implemented when needed, such as for cost predictability, consistency within or across law firms, or for standardized instructions.

Bernie: They are useful, especially as a company grows, but they are not absolutely required, especially where a company has an onsite attorney or patent agent.

Mishra & Chris: There is some benefit to formal processes, especially as not all developers are familiar with IP. One needs to be careful to not get bureaucratic, though. For example, IP review boards that examine disclosures at larger companies are often composed of individuals/disciplines that do not have the background to meaningfully review the material, which leads to inefficiency.

Steven: I am a proponent of formal, written IP policies for some of the reasons I described above. For the upfront time and effort that goes into drafting and adopting a thoughtful, comprehensive IP policy, the company is setting a tone and affirming the value of IP to the company. The company should not neglect the importance of protecting its IP through alternatives to patenting; for example, through trade secret protection. A written IP policy should provide clear guidance regarding the rules and practices that should be implemented and followed to avoid jeopardizing trade secrets. Finally, a clearly written policy is important if an employee acts in a manner adverse or contrary to that policy; the conduct standards set forth may, regrettably, be needed in the event corrective HR action is needed.

Who should be the first hires in a legal and IP department?

Angela: That depends in part on the level of experience of other employees with respect to legal and patent topics. Perhaps the first legal department hire should be a patent attorney, who can work with outside counsel to build the IP portfolio and can also identify when to involve outside counsel in other legal topics.

Bernie: It could be a patent attorney or agent, depending upon how important IP is and how much IP will be generated.

Mishra & Chris: From our perspective as technical folks managing IP, a general counsel may be needed first and foremost. This individual should have a reasonable background in IP. Beyond that, a company's partners and service providers can provide the services needed and there may not be a need for additional staff.

Steven: The most important skills that should be exhibited by a first hire should be issue spotting and risk mitigation. Every attorney has substantive legal subject matter strengths and weaknesses, but the successful attorney, in my experience, is the one who is savvy or self-aware enough to recognize skill-set deficits, but still is able to recognize legal risk or peril to the company.

What do you think about patent committees? Who should be the members and what sort of decision-making process should be put in place? How do you align IP policy with company goals?

Angela: A patent committee can be useful to implement when the IP spend becomes a significant portion of the budget, depending on company interest in building an IP portfolio versus spending on R&D. Senior management

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can balance company benefit versus cost. Trusted members of the R&D team could help in evaluating the usefulness of—or the ability to design around—the inventions submitted.

That said, the time that it takes to organize and convene a patent committee may not be supported by management, and the process may instead be rather ad hoc.

Bernie: They are very useful, but should not dictate all filing decisions. Depending upon the makeup of the company, I would include key innovators, R&D leaders, and business development. I do not think company goals should necessarily drive IP policy, as IP policy has its own logic and timing, which may not align.

Mishra & Chris: Since the vast majority of patents are developed by R&D, the committee should consist of technical thought leaders, some R&D management, and a very small number of business/company executives. Protecting your products should be an implicit goal of any good organization; therefore, IP policy is self-aligning with the company goals.

Steven: Patent committees serve useful roles, but only under certain circumstances. Generally, one is most useful where the company has an active pipeline of invention disclosures that exceed the capacity to convert into filed applications, and invention disclosures need to be prioritized in the context of limited available IP budget. Members should include at least one individual with an understanding of IP law and patent process and at least one individual with the technology background and expertise to understand and distinguish the technical merits of each IDF. Additional contributors might also include an individual with an understanding of the relevant service or product markets who can opine on the competitive or business value of protecting certain product features. A key aspect is the management of the committee, so that it operates efficiently, with sufficient frequency, does not get bogged down in debate, and promotes the company's long-term business and technology interests.

In-house counsel typically step into a role previously held by prior in-house counsel or R&D staff who had been coordinating IP and patents. How do you get up to speed? What are some things to watch out for?

Angela: First, you have to know the IP environment. Obtain a complete docket, map the portfolio visually to understand how all of the applications are related, spot check the work done by in-house and outside counsel, and redistribute work if needed. Pay close attention to the docket and make sure that each item is being handled. Understand what the portfolio already covers to avoid duplicative effort. Evaluate priority and chain of title for the entire portfolio, making corrections as needed.

Meanwhile, get to know the company goals and strategies, management, the R&D community, and the current products in development.

Bernie: I would recommend reading all patents and filed applications, starting with those most recently filed, meeting with key innovators and with any patent committee, and watching out for interpreting the value of patents before you have a full understanding of the product, future planned changes, and competitive outlook.

Steven: Ideally, there should be a hand-off or transition process between prior responsible individuals and new in-house counsel. In practice, this may not always be possible and there may be a gap or break. To mitigate this risk, the company should always have a centralized, accessible, and well-organized repository of documents and information (e.g., a virtual file room), and the responsibility for maintaining and updating its content should fall on each person responsible for in-house IP management.

The industry and science can be fast moving. How do you update overall objectives and the patent portfolio? What should go into a decision to emphasize or de-emphasize resource spend in one area versus others (e.g., let certain patent filings lapse)?

Angela: Because patenting is so expensive, it is important to align the patent budget with company goals. Understand why the company wants patents: Is it to satisfy early-stage investors, prepare an offensive portfolio against competitors, and/or prepare a defensive portfolio against licensing or patent challenges? You build the portfolio based on what it is intended to do, but always remembering that the portfolio must readily adapt as goals change.

For example, if a company goal is to build a portfolio quickly prior to an initial financing round, then multiple continuation applications can be filed in parallel from a single omnibus parent application. If later the goal is to conserve expenditures, continuation filings can be made strategically to minimize cost while maintaining flexibility.

There are also ways to postpone costs, such as filing a PCT national phase application in the U.S. rather than filing parallel U.S. and PCT applications. The filing of Patent Office responses can

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be delayed until just before the initial deadline to stretch out prosecution without paying late fees.

As the company evolves, it must also face difficult decisions about which existing patents and applications to let go. A review of the strength or coverage of individual patent claims can help in culling out weaker ones. Perhaps some patents can be monetized through sale or license, but realistically there is a small chance of being able to recoup the past spend on the patents.

Bernie: Being on site, I can keep up with where the company is going and align objectives based on that reality, both product pipeline and financial realities.

Mishra & Chris: Tracking the competitive space in a weekly search is a key way to spot industry trends. To ensure that relevant IP is filed while minimizing the drain on the organization, the gathering and management of IP should be centralized. By working carefully with external partners and being strategic and opportunistic, the ideas can be collected and filed in an ongoing manner.

Steven: The objectives of the patent portfolio need to be in lockstep with company business objectives, whether the portfolio is being developed for offensive or defensive reasons. The IP manager needs to be in sync with business and technology management and should be included or integrated in strategy meetings. The worst offense that I have seen is expending limited financial resources on patent applications that have no clear nexus or justification in the context of the relevant competitive landscape, product roadmap objectives, or revenue generation objectives. If an IP manager cannot explain in one sentence why a particular patent application represents value to the company, then question why resources are supporting it.

How do you develop and manage an IP budget?

Angela: Make a lot of estimates: the number of new invention disclosures, whether you should expand or contract the portfolio, the number of patents that will soon issue, the number of trademarks and where and in which classes, the number of copyrights or mask works to register, whether you expect to be a party in post-grant review or litigation, whether you will need to add personnel or supporting structure to the internal team, and so forth. Then, based on all of those estimates, you estimate costs for: preparing new patent applications; prosecuting existing applications; filing continuation applications; paying annuities; filing for trademark, copyright, and other IP protection; asserting or defending post-grant review and litigation; and so forth. Then, you may want to add 20-30 percent to provide a margin of error.

Bernie: Much of it is dictated by financing realities and incremental increases over the prior year. The reality is that it is dictated to me and I have to find a way of doing as much as I can with what I am given. Having outside counsel prepare a proposed budget based upon my input has proven to be very effective when the funding is available.

Mishra & Chris: When a company has sufficient history, future spend can be reasonably predicted. In a company's early days, budgeting can be a challenge.

Steven: I manage an IP budget from the perspective of how much IP value I can squeeze out of an IP budget dollar. The main drains on IP budget are outside counsel fees, Patent Office fees, and translation costs. I can moderate or reduce outside counsel fees in several ways: bring more work in-house to salaried IP practitioners; outsource my prosecution workload to lower-cost but highly competent outside counsel; or negotiate caps on outside counsel fees. Patent Office filing fees, particularly PCT/national stage application costs, add up quickly, so be selective regarding which countries or national stage applications to authorize, based on factors such as product market expansion plans.

What are some key organizational tools (such as software) that you use?

Angela: Docketing software is critical to adequately monitor the patent portfolio, once the portfolio exceeds several dozens of applications. This is true whether or not filing is done internally or by outside counsel. As the company grows, a contracts database becomes increasingly necessary.

Bernie: I tend to rely on outside counsel to handle administration and docketing, so I really only rely on that and spreadsheets.

Mishra & Chris: Software tools such as PatSnap are great for our regular searches and general IP management. Google is of course a good resource, as well as the USPTO.

Steven: PatSnap and Orbit Intelligence for patent research and analytics, and Orbit Capture for patent portfolio and workflow management.

Do you use outside support services and if so, what for? What are some things these services do well and what can they do better?

Angela: Outside counsel are leveraged for filing and docketing. In-house legal departments in a start-up are generally not staffed or insured for those responsibilities. Outside counsel can also pick up the slack in patent preparation and prosecution when the internal team does not have bandwidth. The in-house team has the luxury of being in tune with

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the company and product line, so they may be better equipped for preparing comprehensive specifications. On the other hand, outside counsel tends to be more efficient at patent prosecution and better at keeping up to date on changing law and practice. A weakness of outside counsel is the constraint of the billable hour.

Bernie: I rely on outside counsel for docketing, management, and legal issue support and on outside search firms for searching.

What are some other concerns in managing IP development and capture at a growing organization?

Angela: There are those who do not appreciate the value of IP and may not support the cost of protecting IP when that money could instead be used for R&D. It is also quite difficult to enforce policies. For example, there are those who hold the philosophy that everyone should be able to share their ideas for the benefit of humanity, and there are those with a preconception that non-disclosure or confidentiality agreements provide full protection for company technology. Employees are also not always clear about the extent of what is considered confidential. Moreover, employees do not necessarily understand the dangers of phishing and other cyber-attacks, which is especially concerning when employees use their work computers for personal social media or internet browsing.

Bernie: I believe the key concern is how to create and maintain an IP portfolio within the constraints of a company that is constantly looking for funding.

Mishra & Chris: The main concern to us surrounds ensuring that all relevant and important ideas have been filed.

Steven: It is sort of like cultivating a garden—planting seeds and diligently tending to the early shoots will yield fruit in the future! Organization, unity of purpose, and cross-company buy-in and participation are critical, without which a company IP program may founder. An underfunded IP budget will be a gating factor as well, so alignment on IP strategy and objectives among all company stakeholders, whether legal, product development, finance, or sales and marketing, is essential.

Darby Chan is a senior associate in Wilson Sonsini's Palo Alto office and specializes in patent counseling and prosecution for start-up companies in the medical and healthcare technology space.

Angela Murch is Vice President of IP at InCube Labs, LLC, a company that creates and incubates start-ups in the medical device space. She is responsible for all aspects of intellectual property strategy and protection for InCube Labs and the start-ups, in addition to other responsibilities such as drafting and negotiating contracts.

Bernard Shay is General Counsel for Earlens Corporation, where he handles all legal matters, including intellectual property. Earlens is a privately held medical technology company committed to transforming the hearing experience for millions of people who suffer from hearing loss.

Lakshmi Narayan Mishra is a prolific inventor in the neurostimulation arena, with over 20 years of experience and 30 issued U.S. patents to his name. Mishra has worked at Advanced Bionics and Illumina, and currently is Vice President of R&D at Nalu Medical, a privately held early-stage medical device start-up company.

J. Christopher Flaherty is a leading inventor in the field of medical device technology with 30 years of experience and over 230 issued U.S. patents to his name. His patents and applications span a broad range of medical technologies. Chris has been an invited speaker at the USPTO, presenting new technologies. He is President and CEO of Ahee Build Inc., which consults Nalu Medical.

Steven Bowers is a registered patent attorney and Certified Licensing Professional with broad expertise in patent portfolio strategy, IP licensing and transactions, and complex patent litigation. He currently is Vice President of Intellectual Property and Transactions at Exo Imaging, a Silicon Valley start-up developing novel portable ultrasound imaging technologies.

Life Sciences Venture Financings for Wilson Sonsini Clients

By Scott Murano, Partner (Palo Alto)

The table below includes data from life sciences transactions in which Wilson Sonsini Goodrich & Rosati clients participated across the first and second halves of 2020. Specifically, the table compares—by industry segment—the number of closings, the total amount raised, and the average amount raised per closing across the two six-month periods.

	1H 2020	1H 2020	1H 2020	2H 2020	2H 2020	2H 2020
Life Sciences Industry Segment	**Number of Closings**	**Total Amount Raised ($M)**	**Average Amount Raised ($M)**	**Number of Closings**	**Total Amount Raised ($M)**	**Average Amount Raised ($M)**
Biopharmaceuticals	56	$1,627.89	$29.07	51	$1,456.13	$28.55
Genomics	7	$103.32	$14.76	7	$339.98	$48.57
Diagnostics	16	$243.01	$15.19	12	$104.40	$8.70
Medical Devices & Equipment	53	$715.67	$13.50	38	$492.50	$12.96
Health IT	18	$280.77	$15.60	17	$388.58	$22.86
Healthcare Services	17	$359.54	$21.15	17	$641.90	$37.76
Total	**167**	**$3,330.20**		**142**	**$3,423.49**	

The data demonstrates that venture financing activity decreased from the first half of 2020 to the second half of 2020 with respect to the total number of closings, but increased with respect to the total amount raised. Specifically, the total number of closings across all industry segments decreased 15 percent, from 167 to 142, while the total amount raised across all industry segments increased 2.8 percent, from $3,330.20 million to $3,423.49 million.

Notably, the industry segment with the second-largest number of closings during the second half of 2020—medical devices and equipment—experienced a significant decrease in number of closings and total amount raised from the first half to the second half of 2020. Specifically, the number of closings in the medical devices and equipment segment decreased 28.3 percent, from 53 to 38, while the total amount raised decreased 31.2 percent, from $715.67 million to $492.50 million. Similarly, the industry segment with the largest number of closings during the second half of 2020—biopharmaceuticals—saw decreases in both number of closings and total amount raised from the first half to the second half of 2020. Specifically, the number of closings in biopharmaceuticals decreased 8.9 percent, from 56 to 51, while the total amount raised decreased 10.6 percent, from $1,627.89 million to $1,456.13 million.

> From the first half of 2020 to the second half of 2020, the total number of closings across all industry segments decreased 15 percent, while the total amount raised across all industry segments increased 2.8 percent

Meanwhile, the industry segments tied for the third-largest number of closings during the second half of 2020—health IT and healthcare services—experienced a significant increase in total amount raised and little-to-no decrease in number of closings over the same period. Specifically, the total amount raised for health IT increased 38.4 percent, from $280.77 million to $388.58 million, while the total amount raised for healthcare services increased 78.5 percent, from $359.54 million to $641.90 million. The total number of closings for health IT decreased by 5.6 percent, from 18 to 17, while the total number of closings for healthcare services experienced no change, remaining flat at 17. Rounding out the field, diagnostics—the fifth-largest industry segment by number of closings during the second half of 2020—experienced a decrease in both number of closings and total amount raised, and

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Life Sciences Venture Financings for Wilson Sonsini Clients *(Continued from page 6)*

genomics—the smallest industry segment by number of closings during the second half of 2020—experienced no change in number of closings and a huge increase in total amount raised. Specifically, the total number of closings for diagnostics decreased 25 percent, from 16 to 12, while the total amount raised decreased 57 percent, from $243.01 million to $104.40 million. For genomics, the total number of closings for genomics remained at seven from the first half to the second half of 2020, and the total amount raised skyrocketed 229.1 percent, from $103.32 million to $339.98 million.

> Notably, this is the second consecutive six-month period during which average pre-money valuations for life sciences companies increased for all stages of equity financing

In addition, our data suggests that Series A and Series C and later-stage financing activity, in each case as a percentage of all financing activity and measured by number of closings, increased from the first half to the second half of 2020, while Series Seed, Series B, and bridge financing activity all decreased across the same period. The number of Series A closings as a percentage of all closings increased from 16.4 percent to 19.2 percent, and the number of Series C and later-stage closings as a percentage of all closings increased from 15.2 percent to 17.8 percent. Series Seed closings as a percentage of all closings decreased from 11.1 percent to 7.5 percent, Series B closings as a percentage of all closings decreased slightly from 17 percent to 16.4 percent, and bridge financing closings as a percentage of all closings decreased from 28.1 percent to 17.8 percent.

Average pre-money valuations for life sciences companies increased from the first half to the second half of 2020 for all stages of equity financings, including Series Seed, Series A, Series B, and Series C and later-stage financings. For Series Seed financings, the average pre-money valuation increased 3 percent, from $10.60 million to $10.92 million; for Series A financings, it increased 6.7 percent, from $29.76 million to $31.76 million; for Series B financings, it increased 20.9 percent, from $80.81 million to $97.74 million; and for Series C and later-stage financings, it increased 14.3 percent, from $328.1 million to $375.13 million. Notably, this is the second consecutive six-month period during which average pre-money valuations for life sciences companies increased for all stages of equity financing.

Other data taken from transactions in which all firm clients participated in the second half of 2020 suggests that life sciences is the now the second-most active industry for investment among our clients, after having been the most active industry for investment among our clients for several years. During the second half of 2020, life sciences represented 35 percent of total funds raised by our clients, while the software industry represented 44 percent of total funds raised.

Overall, the data indicates that there was less financing activity during the second half of 2020 compared to the first half in terms of number of closings, but the total aggregate amount raised by our life sciences company clients increased marginally during the same period. This is encouraging, considering that the entire second half of 2020 occurred squarely within the pandemic, while only approximately half of the first six months of the year were influenced by the pandemic. Moreover, the closings that did occur were conducted at higher valuations for all stages of equity financing, and it was the second consecutive six-month period where average pre-money valuations increased across the board. This suggests that while investors may be getting pickier, companies that are able to secure financing can leverage their relative attractiveness into higher valuations. We expect the number of closings to improve over the first half of 2021 as the economy begins to emerge from the pandemic.

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U.S.-Japan Healthcare Connection Hosts Conference on "The Coming Revolution in Healthcare"

In April and May, the U.S.-Japan Healthcare Connection—a collaboration between the Japan Society of Northern California (JSNC) and US-Japan Medtech Frontiers (USJMF)—hosted a two-part virtual conference titled "The Coming Revolution in Healthcare." The program showcased the latest developments underlying the transformation of healthcare services through the means of digital delivery, with a particular focus on "hospitals at home" and remote patient monitoring.

The first session, held on April 22 via Zoom, featured a welcome address from JSNC President Takehide Akiyama and lectures from six esteemed guests, including:

- Dr. Fumiaki Ikeno, U.S. Program Director of Japan Biodesign
- Bakul Patel, Director at the Digital Health Center of Excellence of the FDA's Center for Devices and Radiologic Health
- Peter Fitzgerald, M.D., Emeritus Professor of Medicine and Engineering at Stanford University School of Medicine and co-founder and managing partner of Triventures
- Raphael Rakowski, Co-founder and Executive Chairman of Medically Home Company
- Amar Kendale, Chief Product Officer at Teladoc Health
- Zaif Siddiqi, Global Head of 5G and IoT Enterprise Business at NTT DOCOMO Inc.

In addition, the program included a Q&A session in which Dr. Ikeno interviewed three of the guest speakers, Mr. Siddiqi, Mr. Kendale, and Mr. Raphael, as well as a networking session. Click here to view the April 22 session on YouTube.

The second session, held on May 19, featured presentations from representatives of 10 start-ups that showcased their companies' cutting-edge innovations and products. The featured companies included AvodahMed, Casana, CereVu Medical, Digital Diagnostics, Eko Health, Epicore Biosystems, Migraine.AI, Nozomi, Oncoustics, TheraB Medical, and Siren Care. Click here to view the May 19 session on YouTube.

The U.S.-Japan Healthcare Connection strengthens the Silicon Valley/San Francisco Bay Area's links with Japan by identifying and presenting the latest medical technology innovations and anticipated developments. Wilson Sonsini is a founding partner of the U.S.-Japan Healthcare Connection.

Founded in 2013, US-Japan Medtech Frontiers (USJMF) is a Silicon Valley-based nonprofit whose mission is to share best practices for medical device innovation and promote networking and collaboration between U.S. and Japanese medical device organizations. Wilson Sonsini is a co-founder and sponsor of USJMF, and partners Casey McGlynn and Elton Satusky serve on the organization's board of directors, along with Chairman Jack Moorman, Principal at LeVaunt, LLC and Partner at Nichibei MedTech Advisors, LLC; Dr. Fumiaki Ikeno, U.S. Program Director at Japan Biodesign; Kirk Zeller, Partner at Nichibei MedTech Advisors, LLC and Founder of Silicon Prairie Center; and Masa Ishii, Managing Director at AZCA, Inc.

US-Japan MEDTECH FRONTIERS

JAPAN SOCIETY OF NORTHERN CALIFORNIA

Founded in 1905, the Japan Society of Northern California works to advance U.S.-Japan collaboration and understanding in a global context. The Society offers an array of programs and networking opportunities for people and organizations in the Bay Area with a strong interest in Japan.

Biden Administration Inks Bills to Increase Drug Competition

Also Codifies FDA's Longstanding "Active Moiety" Approach for New Chemical Entity Exclusivity

By Eva Yin, Associate (Seattle), and David Hoffmeister, Partner (Palo Alto)

In April 2021, President Biden signed two bipartisan bills that aim to promote drug competition and to reduce prescription drug prices—the Ensuring Innovation Act (EIA)[1] and the Advancing Education on Biosimilars Act of 2021 (Biosimilars Act).[2] While the Biosimilars Act aims to increase patients' and healthcare providers' awareness and adoption of biosimilars by enabling the Department of Health and Human Services to create a website with educational materials about various aspects of biologics and biosimilars, the EIA in part amends the requirements for the New Chemical Entity (NCE) exclusivity under the Federal Food, Drug, and Cosmetics Act (FDCA). This change in the exclusivity provisions has been touted by some as foreclosing the unintended opportunity for drug developers to make certain non-pharmacological changes to previously approved molecules as a way to delay generic drug entry.

In particular, before the EIA amendments, the NCE exclusivity provisions stated that a drug having "no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application" would be eligible for the five-year NCE exclusivity. The EIA amends the statute to replace the phrase "active ingredient (including any ester or salt of the active ingredient)" with "active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations))." Although the U.S. Food and Drug Administration (FDA) has historically interpreted "active ingredient" to mean "active moiety," the courts have not always sided with the FDA in its interpretation of the statute.

The EIA thus adopts the FDA's longstanding "active moiety" approach by incorporating the regulations promulgated by the FDA and also leaving the door open for the FDA to modify the definition or its NCE approach going forward through successor regulations. Since the enactment of the EIA, the FDA has not issued any new guidance or regulation specifically on the NCE exclusivity, but it would not be surprising if the FDA issues new guidance or regulations, especially in view of ongoing litigation in this space.

21 CFR § 314.3 currently defines "active ingredient" and "active moiety" as follows:

> *Active ingredient* is any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or other animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect.
>
> *Active moiety* is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.

Further, the FDA defines a "new chemical entity" under 21 CFR § 314.108 as follows:

> *New chemical entity* means a drug that contains no active moiety that has been approved by FDA in any other NDA submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act.

For drugs where the active ingredient overlaps one-to-one with the active moiety, the NCE analysis is straightforward. On the whole, since the EIA adopts the FDA's longstanding "active moiety" approach, the NCE analysis under the EIA is not expected to impact most drug products going forward. That said, two types of drug products that have been the subject of various litigation are worth taking a closer look in view of the EIA—fixed-combination drug products and prodrugs.

Fixed-Combination Drug Products

Fixed-combination drug products are typically drug products that include two or more active ingredients combined in a single dosage form. In *Amarin Pharm. Ireland Ltd. v. FDA*,[3] the court vacated the FDA's decision to limit the regulatory exclusivity for Amarin's fish oil drug Vascepa to the three-year new clinical

[1] Sen. Bill Cassidy, Press Release, "Cassidy, Smith, Marshall Bipartisan Legislation to Lower Prescription Drug Costs Signed into Law by President" (April 23, 2021), *available at* https://www.cassidy.senate.gov/newsroom/press-releases/cassidy-smith-marshall-bipartisan-legislation-to-lower-prescription-drug-costs-signed-into-law-by-president-; S. 415 (117th Cong.), *available at* https://www.congress.gov/117/bills/s415/BILLS-117s415enr.pdf.

[2] S. 164 (117th Cong.), *available at* https://www.cassidy.senate.gov/imo/media/doc/Advancing%20Education%20on%20Biosimilars%20Act.pdf.

[3] *Amarin Pharm. Ireland Ltd. v. FDA*, 106 F. Supp. 3d 196, 217-19 (D.D.C. 2015); *see also* Congressional Research Service, Defining Active Ingredient: The U.S. Food and Drug Administration's Legal Interpretation of Regulatory Exclusivities (December 10, 2019), *available at* https://crsreports.congress.gov/product/pdf/R/R46110.

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investigation exclusivity instead of the five-year NCE exclusivity. In denying the NCE exclusivity for Vascepa, the FDA argued that Vascepa's active ingredient, icosapent ethyl, which is an ethyl ester of eicosapentaenoic acid (EPA), a type of omega-3 fatty acid, was not eligible as an NCE because the agency previously approved another drug, Lovaza, which composed a mixture of multiple omega-3 fatty acid ethyl esters that included the ester of EPA. The federal judge disagreed with the FDA and held that the FDA improperly equated "active ingredients" with "active moieties" in its evaluation of NCE eligibility for icosapent ethyl and that its "active moiety" approach was contrary to the statute.

The EIA essentially reverses the *Amarin* decision by siding with the FDA and echoes the agency's 2014 Guidance for Industry, titled "New Chemical Entity Exclusivity Determinations for Certain Fixed-Combination Drug Products," stating:[4]

> an application for a fixed-combination submitted under section 505(b) of the FD&C Act will be eligible for 5-year NCE exclusivity if it contains a drug substance, *no active moiety of which has been approved in any other application under section 505(b)*. For example, a fixed-combination drug product that contains a drug substance with a single, new active moiety would be eligible for 5-year NCE exclusivity, even if the fixed-combination also contained a drug substance with a previously approved active moiety.

Accordingly, in order to qualify for the five-year NCE exclusivity, the drug product will need to include at least one active moiety that has never been approved by the FDA. Since the regulatory definition of an active moiety includes "an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule," such modifications or derivatives of a previously approved active moiety would not be eligible for the NCE exclusivity.

Prodrugs

A prodrug typically refers to a drug product that is metabolized or converted into a pharmacologically active form, or a metabolite, in the body. The FDA considers molecules that require metabolic conversion to be active moieties eligible for NCE exclusivity and has granted NCE exclusivity to many prodrugs. For prodrugs involving non-ester covalently bonded molecules of previously approved drugs, their NCE eligibility analysis should not change significantly with the enactment of the EIA.

For example, in a 2009 FDA letter, Docket No. FDA-2009-N-0184,[5] the FDA reaffirmed the five-year NCE exclusivity granted to Vyvanse (lisdexamfetamine dimesylate), a prodrug that consists a non-ester covalent bond between dextroamphetamine and lysine through an amide bond, which is metabolically converted to dextroamphetamine in the body. Dextroamphetamine was an active moiety in a number of previously approved drugs. In this 2009 letter, the FDA provided the following rationale:[6]

> Pursuant to FDA's interpretation of 21 CFR § 314.108, a salt will not be considered an active moiety. Therefore, although lisdexamfetamine dimesylate is the active ingredient of Vyvanse, because lisdexamfetamine dimesylate is a salt, lisdexamfetamine dimesylate is not the active moiety. The exclusivity analysis then turns to the lisdexamfetamine molecule.
>
> As FDA interprets and applies 21 CFR § 314.108, a non-esterified covalently bonded molecule will be considered an active moiety in a drug. FDA has determined that lisdexamfetamine is a non-esterified covalently bonded molecule and thus lisdexamfetamine is the active moiety in Vyvanse. Further, lisdexamfetamine has not been previously approved as an active moiety in a drug product under section 505(b) of the Act, and is therefore a new chemical entity entitled to 5 years of exclusivity.

Further, the FDA clarified that it "relies on a relatively straightforward analysis of the chemical structure of the drug when analyzing eligibility for exclusivity," distinguishing its current position from a 1991 NCE exclusivity decision made based on the molecule's activity before the agency finalized the applicable regulations.[7] In the 1991 decision, the FDA granted the NCE exclusivity to an ester of a previously approved molecule on the basis that the esterified portion of the molecule was responsible for the molecule's activity while the de-esterified form was inactive. Such activity-based ester modification of a previously approved molecule would not be eligible for the NCE exclusivity under the current chemical structure analysis and regulations.

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[4] FDA, Guidance for Industry, New Chemical Entity Exclusivity Determinations for Certain Fixed-Combination Drug Products (October 2014), *available at* https://www.fda.gov/files/drugs/published/New-Chemical-Entity-Exclusivity-Determinations-for-Certain-Fixed-Combination-Drug-Products.pdf (emphasis added).

[5] FDA, Letter dated October 23, 2009, Docket No. FDA-2009-N-0184, *available at* https://www.wsgr.com/a/web/8e7awFcT8F2CVNDVVDbdeP/fda-2009-n-0184-00341.pdf.

[6] *Id*. at 9-10.

[7] *Id.* at 9.

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Consistent with the FDA's rationale in the *Vyvanse* decision, the EIA aligns the statutory language with the FDA's regulations and makes it more clear that prodrugs consisting of esters, salts, or other noncovalent derivatives of a previously approved active moiety would no longer be eligible for the NCE exclusivity.

***Sandoz v. FDA*—Dust Not Yet Settled**

However, a recent complaint filed by Sandoz on March 5, 2021, against the FDA in the District Court for the District of Columbia, before the enactment of the EIA, challenging the FDA's grant of the NCE exclusivity for Sanofi's multiple sclerosis drug Aubagio (teriflunomide), highlights the complexity and the nuance of the NCE analysis.[8] This complaint comes after Sandoz's previous administrative appeal of the FDA's NCE exclusivity decision on Aubagio and filing of abbreviated new drug applications (ANDAs) for its generic version.

Unlike the *Vyvanse* case, the previously approved active moiety involved here, leflunomide, is the prodrug, and the NCE designation being challenged is the metabolite, which was present as an impurity in the previously approved prodrug. Upon oral administration of leflunomide, the isoxazole ring of leflunomide is opened to form the teriflunomide metabolite in the body.[9]

According to the complaint, Sandoz argues that the FDA had previously approved leflunomide as the active ingredient of Arava in 1998 for a different indication and that "what is highly unusual and pivotally important to this case is the fact that teriflunomide not only is the active metabolite of Arava®'s leflunomide in vivo; it also is meaningfully present in Arava® tablets ex vivo … FDA-approved Arava® tablets contain therapeutically active teriflunomide that at least in part is responsible for Arava®'s physiological and pharmacological action."[10]

In granting the NCE exclusivity for Aubagio, the FDA argued that teriflunomide has not been previously approved and was thus eligible for the NCE exclusivity, which is in line with the FDA's chemical structure analysis for the active moiety in the drug product. This case, however, highlights the potential ambiguity created where both the FDA and the drug sponsor were aware of the presence of the metabolite in a previously approved drug product, albeit as an impurity, even though the active ingredient previously approved by the FDA was leflunomide. The outcome of this case has the potential to muddy the waters or provide further clarity to the NCE analysis, especially with respect to the scope of the definition of active moiety in the prodrug context and known impurities that are later discovered to have physiological or pharmacological activity.

In other areas, the Biden administration has moved quickly to restore FDA oversight and independence in its regulation of various medical products, and the enactment of the EIA is no exception.

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[8] *Sandoz Inc. v. Cochran et al.*, No. 1:21-cv-00600 (D.D.C. 2021).
[9] Aly L, Hemmer B, and Korn T, "From Leflunomide to Teriflunomide: Drug Development and Immunosuppressive Oral Drugs in the Treatment of Multiple Sclerosis," *Curr Neuropharmacol*, 2017;15(6):874-891, *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5652031/.
[10] Complaint at ¶¶ 31-33, No. 1:21-cv-00600.

FDA REGULATORY EXCLUSIVITIES

New Chemical Entity Exclusivity - 5 years

- For a drug that contains a new active moiety not previously approved under section 505(b)

New Clinical Investigation Exclusivity - 3 years

- For a drug with a previously approved active ingredient where the application or supplement contains reports of a new clinical investigation (not including bioavailability studies) conducted or sponsored by applicant and that is essential for approval (e.g., new formulation or new indication of a previously approved drug)

Biologic Exclusivity - 12 years

- For first licensure (BLA) of a biologic product

Orphan Drug Exclusivity - 7 years

- For diseases or conditions affecting fewer than 200,000 in the U.S. (or no hope of recovering costs if > 200,000)

Pediatric Exclusivity - 6 months added to patents and/or exclusivities

- 6 months of market protection added at the end of listed patents and/or exclusivities for a sponsor's drug products containing the same active moiety
- Awarded when the sponsor has conducted and submitted a pediatric study on the active moiety in accordance with a Written Request from the FDA

Generating Antibiotic Incentives Now (GAIN) Exclusivity - 5 years added to exclusivities

- For certain new antibiotic drugs for specific infectious diseases

Select Recent Life Sciences Client Highlights

Day One Pharmaceuticals Announces Closing of Initial Public Offering

On June 1, Day One Biopharmaceuticals, Inc., a clinical-stage biopharmaceutical company dedicated to developing and commercializing targeted therapies for patients of all ages with genetically defined cancers, announced the closing of its initial public offering of 11,500,000 shares of its common stock, including the full exercise of the underwriters' option to purchase up to 1,500,000 additional shares of common stock, at a public offering price of $16.00 per share. The gross proceeds from the offering, before deducting underwriting discounts and commissions and other offering expenses payable by Day One, were $184 million. The shares began trading on the Nasdaq Global Select Market on May 27 under the ticker symbol "DAWN." Wilson Sonsini advised Day One on IP matters related to the transaction.

Centessa Announces Pricing of Initial Public Offering

On May 27, Centessa Pharmaceuticals, a clinical-stage company employing its innovative asset-centric business model to discover, develop, and ultimately deliver impactful medicines to patients, announced the pricing of its initial public offering of 16,500,000 American Depositary Shares (ADSs), each representing one ordinary share at a public offering price of $20.00 per ADS. All of the ADSs are being offered by Centessa. The gross proceeds to Centessa from the offering, before deducting underwriting discounts, commissions, and other estimated offering expenses, are expected to be approximately $330 million. The shares began trading on the Nasdaq Global Select Market on May 28 under the ticker symbol "CNTA." Wilson Sonsini advised Centessa on patent matters related to the IPO.

Emboline Raises Over $55 Million in Series D Funding

On May 25, Emboline, Inc., a privately held medical device company focused on reducing stroke and other damage caused by embolic debris released during transcatheter heart procedures, announced the closing of its Series D funding of over $55 million. The funding was led by new investors Matrix Capital Management and an undisclosed strategic investor, with additional participation by existing investors, including SV Tech, ShangBay Capital, and Global Assets Investment. The investment will support a planned U.S.-based pivotal trial for FDA approval as well as investigational studies for new indications, and manufacturing and commercial operations for the Emboliner.™ Wilson Sonsini represented Emboline in the transaction.

Aerpio Pharmaceuticals and Aadi Bioscience Enter into Definitive Merger Agreement

On May 17, Aerpio Pharmaceuticals, a biopharmaceutical company focused on developing compounds that activate Tie2, and Aadi Bioscience, a biopharmaceutical company focusing on precision therapies for genetically defined cancers with alterations in mTOR pathway genes, announced they have entered into a definitive merger agreement. They will form a public company focused on advancing Aadi's lead product candidate, FYARROTM. Following the proposed merger, Aerpio will change its name to "Aadi Bioscience." In support of the merger, Aerpio has entered into subscription agreements to raise $155 million in a private investment in public equity (PIPE) financing. The PIPE financing is expected to be consummated concurrently with the closing of the merger. Wilson Sonsini represented Aadi Biosciences in the transaction.

Biogen and Capsigen Announce Strategic Research Collaboration

On May 10, Biogen Inc. and Capsigen Inc. announced they have entered into a strategic research collaboration to engineer novel adeno-associated virus (AAV) capsids that have the potential to deliver transformative gene therapies that address the underlying genetic causes of various CNS and neuromuscular disorders. Under the terms of the agreement, Biogen will receive an exclusive license under Capsigen's proprietary technology for an undisclosed number of CNS and neuromuscular disease targets. Capsigen will receive a $15 million upfront payment and is eligible to receive up to $42 million in potential research milestones and up to an additional $1.25 billion in potential development and commercial payments. Capsigen is also eligible to receive royalties on future net sales of products that incorporate capsids resulting from the collaboration. Wilson Sonsini advised Capsigen on IP matters related to the collaboration.

Ceribell Completes $53 Million Series C Financing

On April 29, Ceribell, innovator of the Rapid Response EEG™, a novel non-invasive brain monitor, announced the completion of a $53 million Series C financing, which was co-led by Longitude Capital and The Rise Fund. Other new investors included RA Capital Management, Redmile Group, and Red Tree Venture Capital, with additional support from existing shareholders. Ceribell will use the financing proceeds to further expand its commercial footprint in emergency departments and intensive care units globally. Wilson Sonsini represented Ceribell in the transaction.

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Forge Biologics Announces Closing of $120 Million Series B Financing
On April 29, Forge Biologics, a gene therapy-focused contract development and manufacturing organization, announced the closing of a $120 million Series B financing. The round was led by RA Capital Management with participation from Perceptive Advisors and related affiliates, Surveyor Capital (a Citadel company), Octagon Capital, and Marshall Wace. Existing investors Perceptive Xontogeny Venture Fund and Drive Capital also participated. Forge will use the proceeds to accelerate the expansion of its AAV manufacturing CDMO capabilities with cGMP production capacity, as well as operate its subsidiaries that are advancing novel AAV gene therapy programs. Wilson Sonsini advised RA Capital on corporate and IP matters related to the financing.

Pfizer Acquires Amplyx Pharmaceuticals
On April 28, Pfizer Inc. announced that it has acquired Amplyx Pharmaceuticals, Inc., a privately held company dedicated to the development of therapies for debilitating and life-threatening diseases that affect people with compromised immune systems. Amplyx's lead compound, Fosmanogepix (APX001), is a novel investigational asset under development for the treatment of invasive fungal infections. In addition to Fosmanogepix, with this acquisition, Pfizer has secured ownership of Amplyx's early-stage pipeline that includes potential antiviral (MAU868) and antifungal (APX2039) therapies. Wilson Sonsini advised Amplyx on IP matters related to the transaction.

Boundless Bio Raises Oversubscribed $105 Million Series B Financing
Also on April 28, Boundless Bio, a next-generation precision oncology company developing innovative therapeutics directed against extrachromosomal DNA (ecDNA) in aggressive cancers, announced the closing of an oversubscribed $105 million Series B financing. RA Capital Management and Nextech Invest co-led the financing, with participation from a top-tier syndicate of funds, including Fidelity Management & Research Company LLC, Redmile Group, Wellington Management, Surveyor Capital (a Citadel company), PFM Health Sciences, and Logos Capital, along with a group of current investors. Wilson Sonsini advised Boundless Bio on IP matters related to the transaction.

Recursion Pharmaceuticals Announces Closing of $501 Million IPO
On April 21, Recursion Pharmaceuticals, a clinical-stage biotechnology company decoding biology by integrating technological innovations across biology, chemistry, automation, data science, and engineering, announced the closing of its initial public offering of 27,878,787 shares of its Class A common stock, which includes the exercise in full of the underwriters' option to purchase 3,636,363 additional shares of its Class A common stock, at a price to the public at $18.00 per share. Including the option exercise, the gross proceeds from the offering were $501.8 million, before deducting underwriting discounts and commissions and other offering expenses payable by Recursion. The shares began trading on the Nasdaq Global Select Market on April 16 under the symbol "RXRX." Wilson Sonsini advised Recursion on the transaction.

Janux Therapeutics Closes $125 Million Series B Financing
On April 20, Janux Therapeutics announced the closing of a $125 million Series B financing led by RA Capital Management and joined by new investors BVF Partners L.P., EcoR1 Capital, Hartford HealthCare Endowment, Janus Henderson Investors, Logos Capital, Samsara BioCapital, and Surveyor Capital (a Citadel company). Existing investors OrbiMed, Avalon Ventures, and Bregua also participated. The proceeds of the financing will help support the advancement of Janux's pipeline of next-generation T cell engager immunotherapies into initial proof of concept clinical trials. Wilson Sonsini advised Janux on IP matters related to the transaction.

Tango Therapeutics and BCTG Acquisition Corp. Announce Merger Agreement
On April 14, Tango Therapeutics, a biotechnology company committed to discovering and delivering the next generation of precision cancer medicines, and BCTG Acquisition Corp., a special purpose acquisition company (SPAC) sponsored by Boxer Capital, announced they have entered into a definitive merger agreement. Upon the closing of the transaction, the company will be named Tango Therapeutics, Inc. Tango Therapeutics, Inc. common stock is expected to be listed on Nasdaq under the ticker symbol "TNGX." Wilson Sonsini served as patent counsel to BCTG Acquisition Corp. in the transaction.

Arcellx Closes $115 Million Series C Financing
On April 13, Arcellx, a privately held clinical-stage biopharmaceutical company, announced that it raised $115 million in a Series C financing to advance its pipeline of adaptive and controllable cell therapies. The proceeds will support the company's development of CART-ddBCMA, a BCMA-specific CAR-modified T-cell therapy currently in Phase 1 and anticipated to begin a pivotal trial in 2022. In addition, the funding

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will support initiation of clinical trials evaluating ACLX-001 and ACLX-002, cell therapies derived from Arcellx's uniquely controllable ARC-SparX platform, in multiple myeloma (MM) and acute myelogenous leukemia (AML), respectively. Wilson Sonsini advised Arcellx on the transaction.

Crinetics Pharmaceuticals Announces Closing of Common Stock Offering
On April 12, Crinetics Pharmaceuticals, Inc., a clinical-stage pharmaceutical company focused on the discovery, development, and commercialization of novel therapeutics for rare endocrine diseases and endocrine-related tumors, announced that it has closed its previously announced underwritten follow-on offering of 4,562,044 shares of its common stock at a price to the public of $16.44 per share. The gross proceeds to Crinetics from the offering, before deducting the underwriting discounts and commissions and other offering expenses, were approximately $75 million. Wilson Sonsini advised Crinetics on patent matters related to the transaction.

Reneo Pharmaceuticals Announces Pricing of Initial Public Offering
On April 8, Reneo Pharmaceuticals, Inc., a clinical-stage pharmaceutical company focused on the development and commercialization of therapies for patients with rare, genetic, mitochondrial diseases, announced the pricing of its initial public offering of 6,250,000 shares of its common stock at a public offering price of $15.00 per share, for total gross proceeds of approximately $93.8 million, before deducting underwriting discounts and commissions and offering expenses. The shares began trading on the Nasdaq Global Market on April 9 under the symbol "RPHM." Wilson Sonsini advised Reneo on patent matters related to the transaction.

Applied Molecular Transport Announces Pricing of Initial Public Offering of Common Stock
On March 31, Applied Molecular Transport (AMT), a clinical-stage biopharmaceutical company leveraging its proprietary technology platform to design and develop a pipeline of novel biologic product candidates to treat autoimmune, inflammatory, metabolic, and other diseases, announced the pricing of an underwritten public offering of 2,500,000 shares of its common stock at a public offering price of $42.00 per share. The gross proceeds to AMT from the offering, before deducting underwriting discounts and commissions and other offering expenses payable by AMT, were expected to be $105 million. Wilson Sonsini advised AMT on the transaction.

Lifelink Systems Completes $9.75 Million Series A Funding Round
On March 30, Lifelink Systems announced that it has completed its Series A funding round, raising $9.75 million to accelerate the growth of its conversational AI technology for healthcare enterprises. The financing was led by DigiTx Partners and included Primera Capital, Baleon Capital, and inside investors. Lifelink Systems runs a conversational AI technology platform used by large healthcare provider systems and life sciences companies to improve the way they interact with patients. Wilson Sonsini advised Lifelink Systems on the transaction.

Design Therapeutic Announces Closing of IPO
On March 30, Design Therapeutics, Inc., a biotechnology company developing a platform of gene targeted chimera (GeneTAC™) small molecules for the treatment of serious degenerative disorders caused by inherited nucleotide repeat expansions, announced the closing of its previously announced initial public offering of 13,800,000 shares of its common stock, which includes 1,800,000 shares sold pursuant to the exercise in full by the underwriters of their option to purchase additional shares, at a price to the public of $20 per share. The aggregate gross proceeds to Design from the offering were approximately $276 million, before deducting underwriting discounts and commissions and offering expenses. The shares began trading on the Nasdaq Global Select Market on March 26 under the ticker symbol "DSGN." Wilson Sonsini advised Design on patent matters related to the transaction.

Tempest and Millendo Announce Proposed Merger Agreement
On March 29, Tempest Therapeutics, Inc., a privately held clinical-stage oncology company developing potentially first-in-class therapeutics that combine both targeted and immune-mediated mechanisms, and Millendo Therapeutics, Inc., announced that they have entered into a definitive agreement under which Millendo will merge with Tempest in an all-stock transaction. Upon shareholder approval, the combined company is expected to operate under the name Tempest Therapeutics and trade on the Nasdaq Capital Market under the ticker symbol "TPST." In support of the merger, Tempest has secured commitments from a premier syndicate of healthcare investors for a $30 million PIPE financing that is expected to close concurrent with the completion of the merger. Wilson Sonsini advised Tempest on patent matters related to the transactions.

Everlywell Acquires PWNHealth and Home Access Health Corporation
On March 24, Everlywell, a leading digital health company, announced that it has acquired PWNHealth and Home Access Health Corporation and formed parent company Everly Health. Together, the combined companies support more

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than 20 million people annually in all 50 U.S. states, Canada, and Puerto Rico. In May 2020, Everlywell became the first digital health company to receive FDA authorization for a mail-in COVID-19 test and is one of the first companies to receive "direct to consumer" (DTC) authorization from the FDA for its COVID-19 Test Home Collection Kit DTC. Wilson Sonsini advised Everlywell on the acquisition.

4D pharma plc Announces Completion of Merger with Longevity Acquisition Corporation

On March 22, 4D pharma plc, a Leeds, UK-based pharmaceutical company leading the development of Live Biotherapeutic products (LBPs)—a novel class of drugs derived from the microbiome—announced the completion of its merger with Longevity Acquisition Corporation, a Nasdaq-listed special purpose acquisition company (SPAC). The merger was structured as an acquisition of the SPAC by 4D pharma, a concurrent global PIPE financing, and the concurrent Nasdaq listing of 4D pharma American Depositary Shares and warrants. Wilson Sonsini advised 4D pharma on corporate and intellectual property matters related to the cross-border transaction.

Savara Announces Closing of $130 Million Public Offering

On March 15, Savara Inc., an orphan lung disease company, announced the closing of an underwritten public offering of 57,479,978 shares of its common stock, including 11,694,150 shares sold pursuant to the exercise in full by the underwriters of their option to purchase additional shares, at a price to the public of $1.45 per share. In addition, Savara sold to certain investors pre-funded warrants to purchase an aggregate of 32,175,172 shares of common stock at a purchase price of $1.449 per warrant. As a result of the underwriters' full option exercise, the aggregate gross proceeds of the offering to Savara, before deducting underwriting discounts and commissions and other offering expenses, were approximately $130 million. Wilson Sonsini advised Savara in the transaction.

Prometheus Biosciences Announces Upsized Pricing of IPO

On March 11, Prometheus Biosciences, a biotechnology company pioneering a precision medicine approach for the discovery, development, and commercialization of novel therapeutic and companion diagnostic products for the treatment of inflammatory bowel disease, announced the pricing of its upsized initial public offering of 10,000,000 shares of common stock at a public offering price of $19.00 per share. The shares began trading on the Nasdaq Global Select Market on March 12 under the ticker symbol "RXDX." The gross proceeds from the offering, before deducting underwriting discounts and commissions and other offering expenses payable by Prometheus, are expected to be $190 million. Wilson Sonsini advised Prometheus on IP matters related to the transaction.

Ventyx Biosciences Raises $114 Million Financing

On March 9, Ventyx Biosciences, a clinical-stage biotechnology company advancing a pipeline of immune modulators to treat inflammatory diseases and autoimmune disorders, announced the completion of a $114 million equity financing. The financing was led by venBio Partners alongside investors including Third Point, RTW Investments, Janus Henderson Investors, Wellington Management, OrbiMed, Surveyor Capital, Farallon Capital, Vivo Capital, Logos Capital, Qiming Venture Partners USA, and Cormorant Asset Management. Founding investor New Science Ventures also participated. Wilson Sonsini advised Ventyx Biosciences on corporate and patent matters related to the transaction.

Janux Therapeutics Announces $56 Million Series A

On March 3, Janux Therapeutics, a developer of safe, effective novel immunotherapies using its proprietary Tumor Activated T Cell Engager (TRACTr) technology, announced the close of a $56 million Series A financing. The financing was led by Avalon Ventures and joined by new investors OrbiMed and RA Capital Management, as well as existing investors Bregua and Correlation Ventures. Wilson Sonsini advised Janux on patent matters related to the transaction.

WuXi AppTec Completes Acquisition of OXGENE

On March 2, WuXi AppTec, a leading global provider of R&D- and manufacturing-enabling services in the pharmaceutical, biotechnology, and medical device industries, announced that it has completed its acquisition of OXGENE, a pioneering UK-based contract research and development organization that designs and develops scalable gene therapy technologies. The acquisition enables WuXi AppTec to offer its customers end-to-end support in the creation and development of cutting-edge cell and gene therapies for patients in need worldwide. Wilson Sonsini represented WuXi AppTec in the transaction, in collaboration with Taylor Wessing.

Cullgen Closes $50 Million Series B Investment

On February 25, Cullgen Inc., a leading biotechnology company developing small molecule therapeutics based on its proprietary uSMITE™ platform of targeted protein degradation technology, announced that it has closed a $50 million Series B financing. In addition to receiving funding from

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existing investors, five new prominent international VC firms also participated in the financing, including the lead investor, 3E Bioventures Capital, as well as Heights Capital Management (an affiliate of Susquehanna International Group), Octagon Capital, MSA Capital, and South China Venture Capital. Wilson Sonsini advised Cullgen on patent matters related to the transaction.

NuVasive Acquires Simplify Medical
On February 24, NuVasive, Inc., the leader in spine technology innovation focused on transforming spine surgery with minimally disruptive, procedurally integrated solutions, announced that it has acquired Simplify Medical, a privately held company and developer of the Simplify® Cervical Artificial Disc (Simplify Disc) for cervical total disc replacement (cTDR). The acquisition adds the most clinically effective cTDR technology and further distinguishes NuVasive's cervical portfolio in the market. Wilson Sonsini represented Simplify Medical in the transaction.

Vividion Announces $135 Million Series C Financing
On February 24, Vividion Therapeutics, Inc., a biotechnology company utilizing novel discovery technologies to unlock high-value, traditionally undruggable targets with precision therapeutics for devastating cancers and immune disorders, announced the completion of a $135 million Series C financing. The financing was co-led by new investors Logos Capital and Boxer Capital of Tavistock Group. Wilson Sonsini advised Vividion in patent matters related to the financing.

Regor Therapeutics Announces Completion of $90 Million Series B Financing
On February 18, Regor Therapeutics, a clinical-stage biotechnology company dedicated to the discovery of innovative medicines to treat cancer, immune disorders, and metabolic diseases, announced the completion of a $90 million Series B financing. The financing was led by Lilly Asia Ventures and included participation from Loyal Valley Capital, Lanting Capital, TF Capital, and Vertex Ventures China. Wilson Sonsini advised Lilly Asia Ventures on IP matters related to the transaction.

Excision BioTherapeutics Completes $60 Million Financing
On February 17, Excision BioTherapeutics, a leading developer of potentially curative CRISPR anti-viral therapies to improve patient lives, announced the completion of a $60 million financing. The proceeds will be used to advance Excision's lead candidate, EBT-101, into a Phase 1/2 clinical trial in patients with chronic HIV infection. The financing will also support preclinical programs including EBT-103 targeting JC Virus for Progressive Multifocal Leukoencephalopathy (PML), EBT-104 for Herpes Simplex Virus, and EBT-107 for Hepatitis B. Wilson Sonsini advised Excision on IP matters related to the financing.

Centessa Pharmaceuticals Launches with $250 Million Series A Financing
On February 16, Centessa Pharmaceuticals launched as a novel asset-centric pharmaceutical company designed and built to advance a portfolio of highly validated programs. Centessa's asset-centric R&D model applied at scale has assembled best-in-class or first-in-class assets, each of which is led by specialized teams committed to accelerate development and reshape the traditional drug development process. The company was founded by Medicxi and raised $250 million in an oversubscribed Series A financing led by General Atlantic and co-led by Vida Ventures and Janus Henderson Investors. Wilson Sonsini advised General Atlantic on patent matters related to the transaction.

Q'Apel Medical Raises $22 Million
On February 11, Q'Apel Medical, an innovative neurovascular company specializing in developing and commercializing novel access device technology for vascular interventions, announced that it has raised $22 million in Series C funding. The round included River Cities Capital, Soleus Capital, and incumbent investor Research Corporation Technologies (RCT). Q'Apel Medical products are being utilized in over 130 hospital systems nationwide. Wilson Sonsini advised Q'Apel Medical on the transaction.

Day One Announces $130 Million Series B Financing
On February 10, Day One Biopharmaceuticals, a clinical-stage biopharmaceutical company focused on accelerating new, promising targeted therapies for children and adults with cancer, announced a $130 million Series B financing from leading life sciences investors. With the completion of the Series B financing, Day One has raised more than $190 million from leading life science investors since the company initiated operations in late 2019. Wilson Sonsini advised Day One on IP matters related to the transaction.

Pacific Biosciences Announces $900 Million Investment from SoftBank
On February 10, Pacific Biosciences, a leading provider of high-quality, long-read sequencing platforms, announced that SB Management, a subsidiary of Softbank Group Corp., will make an investment of $900 million in convertible senior notes to support the company's future growth initiatives. Under the terms of the investment, SB Management will purchase a total aggregate principal amount of $900 million in convertible senior notes due

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2028. The notes will have an initial conversion price of $43.50 per share of the company's common stock, subject to customary anti-dilution and other adjustments. Wilson Sonsini advised Pacific Biosciences in the transaction.

Nautilus Biotechnology to List on Nasdaq Through Merger with Arya Sciences Acquisition Corp III
On February 8, Nautilus Biotechnology, Inc., a biotechnology company pioneering a single-molecule protein analysis platform for quantifying the human proteome, and Arya Sciences Acquisition Corp III, a special purpose acquisition company (SPAC) sponsored by Perceptive Advisors, announced that they have entered into a definitive business combination agreement. In addition to the approximately $150 million held in Arya III's trust account, a group of premier healthcare investors has committed to participate in the transaction through a common stock PIPE of approximately $200 million. Upon the closing of the transaction, Arya III will redomicile as a Delaware corporation and be renamed Nautilus Biotechnology. Wilson Sonsini advised Nautilus Biotechnology on the transaction.

Engrail Therapeutics Acquires NeuroCycle Therapeutics
On February 2, Engrail Therapeutics announced that it has acquired NeuroCycle Therapeutics, a company focused on sub-type selective GABA-A modulation. The acquisition strengthens Engrail's presence in the GABA-A space and provides a strong platform for initiation of clinical trials with multiple assets in 2021. Founded in 2019, Engrail is forging a new direction to reduce the burden of diseases that impact the nervous system. Wilson Sonsini represented NeuroCycle Therapeutics in the transaction.

Upcoming Life Sciences Events

Wilson Sonsini's 28th Annual Medical Device Conference (Virtual)
June 24-25, 2021
8:00 a.m. – 6:00 p.m. Pacific
https://mdc.wsgrevents.com/

This year's two-day virtual Medical Device Conference will feature a variety of panel sessions in the morning and partnering meetings throughout the day. In a series of topical panels, industry CEOs, venture capitalists, industry strategists, investment bankers, and market analysts will provide insight on topics such as next-generation medical device innovation, AI in healthcare, COVID-19's impact, and SPACs and traditional IPOs. Meanwhile, the Partnering Hall will provide personalized opportunities for investors and large medtech companies to meet with start-ups that are searching for and pursuing potential investment, partnering, and acquisition opportunities. We will once again collaborate with MedTech Innovator, the industry's nonprofit global competition and accelerator for medical device, digital health, and diagnostic companies, to highlight 50 best-in-class start-ups from around the world.

Whether you're a medtech entrepreneur, the CEO of a venture-backed company, a business development executive from a large company, an angel investor, a venture capitalist, or a corporate investor, don't miss this exciting and dynamic virtual conference focused on helping you craft a winning strategy to tackle any challenge the year may bring.

Save the Date - Phoenix 2022: The Medical Device and Diagnostic Conference for CEOs
October 19-21, 2022
The Ritz-Carlton, Half Moon Bay
Half Moon Bay, California
https://phoenix.wsgrevents.com/

Our annual Phoenix Conference has long provided medical device and diagnostic executives with an unrivaled experience that helps to inform and shape company strategy for the years ahead. Though we have decided to postpone this year's event, we are excited to announce that we will hold the next Phoenix Conference in October 2022 at The Ritz-Carlton, Half Moon Bay. At that time, we will bring the medtech community together for a lively celebration of the industry's incredible, life-saving work throughout the pandemic, as well as an in-depth discussion of where the sector is headed in the coming years. We wish you and yours continued good health, and we look forward to seeing you in Half Moon Bay in 2022!

Casey McGlynn, a leader of the firm's life sciences practice, has editorial oversight of *The Life Sciences Report* and was assisted by Elton Satusky, Scott Murano, James Huie, and Eric Hsu. They would like to take this opportunity to thank all of the contributors to the report, which is published on a semi-annual basis.

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