

Building The Biotech City: Is Los Angeles The Go-To Destination For Tomorrow's Drug Innovations?

Round Table Discussion: Positioning Los Angeles As The Next Big Biotech Hub

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Executive Summary

The complexity of producing viable drug candidates is increasing as an abundance of new science keeps extending the range of possible targets and fragmenting disease subtypes. Proximity to novel exploratory research is a driver of pipeline productivity – so can physical location within a communal geography of well-resourced intellectual firepower raise the odds for R&D success? *In Vivo* sits down with eight key leaders in academia, VC, commercial real estate and groundbreaking biotech to discuss how Los Angeles – the “out there” city of out-sized ambitions – is positioning itself for global leadership in the curative technologies of the future.



NEXT STOP FOR BIOTECH? LOS ANGELES

Home to 10 million people, Los Angeles county is a global economic power in its own right, with an equivalent rank of 13th among the 36 Organization for Economic Co-operation and Development (OECD) industrialized countries by annual gross domestic product (GDP). Local researchers received more than \$1bn in new grants from the National Institutes of Health (NIH) in 2018, among the highest in the country. The biosciences sector employs more than 90,000 people, with chart-topping average wages at \$83,000 plus, and with disproportionately strong job growth in high value-added research and laboratory services.

The Roundtable group identified as positives LA's extensive university network with a strong entrepreneurial orientation, a deep presence in adjacent sectors like digital health, clinical expertise in managing trial work in diverse populations and ready access to funding for early-stage science. Deficits include the absence of a single geographic center of gravity in a region where transport links are tenuous, scarcity (and the high cost) of available private-sector lab space, lack of a local VC community committed to late-stage funding and a shortage of experienced management talent. Progress is being made on the latter two, especially with the recent launch of at least two new VC firms with a "geo-centric" investing philosophy.

So what? The city's successful bid for the 2028 Summer Olympics and Paralympics provides a global spotlight and rallying point for outsized re-branding initiatives that could prove more enduring in terms of human impact than the games themselves – like positioning Los Angeles as the biotech hub of tomorrow. Is big pharma ready to step up to the plate?

Q In Vivo: Los Angeles is the geography of destiny, with an expanding and diverse economy whose output now exceeds \$900bn annually, placing it third, after Tokyo and New York, among world metropolitan areas with the biggest economic footprint. As a scene setter, how did you land in Los Angeles – as a knowledge leader, what is the value-added to being in this part of the country?

A **Arie Beldegrum, co-founder and executive chair, Allogene Therapeutics:** I received my medical degree in Israel and did my residency at Harvard University followed by a surgical oncology fellowship at the National Cancer Institute (NCI) under Dr. Steve Rosenberg, a mentor who stirred my early interest in immunotherapy as a treatment pathway for cancer. Back in the 1980s, few institutions were either attracted to this area or had embraced its potential, but I learned quickly that UCLA was the exception. As a result, I joined the medical school faculty as an assistant professor in urologic surgery and signed on as a researcher at the university's Jonsson Comprehensive Cancer Center. With several colleagues who, like me, remain on the UCLA faculty today, we worked to raise the profile of cancer immunotherapy and gene therapy research by soliciting joint grants from the National Institutes of Health (NIH) and other granting agencies.

A The funding we received helped set the stage for the discovery of revolutionary new medicines that use the body's own defense mechanisms to attack cancer cells. It also gave me the confidence in our science and the ability to take the calculated risks of investing in and founding several business ventures here in Los Angeles aimed at bettering the lives of patients with advanced or incurable cancers.



Participants, left to right: Ken Schultz, Trethera Inc; Steve Rosen, City of Hope; Beth Seidenberg, Westlake Village BioPartners; Amir Nalberg, UCLA Technology Development Group; Arie Belldegrun, Allogene Therapeutics; William Looney, In Vivo; Mike Jung, UCLA Chemistry Dept; Monica Schmiede, Informa Pharma Intelligence; David Reese, Amgen. Not pictured: Peter Moglia, Alexandria Real Estate Equities.

q As an aside, what led you to make that decision to combine the practice of medicine with business entrepreneurship? What was the chronology of your success as arguably the man who made Los Angeles a magnet for research on new ways to fight cancer?

A **Belldegrun:** The NCI grant money was great, but I realized that academic research had limitations. Even assuming your work could get published, the immediate impact on patients was negligible. So, in 1996, I decided to start a biotech company, called Agensys, with a mission to discover and commercialize novel monoclonal antibodies to treat solid tumor cancers. In launching Agensys, I relied on support from a group of fellow professors at the UCLA Medical School who joined me as the scientific founders of the company. It was the reason why we chose nearby Santa Monica as the site for our headquarters. The decision proved fortuitous when, in 2007, Japan's Astellas Pharma tendered a buyout offer. The new owners subsequently made a significant new investment in research and manufacturing at the Santa Monica location. This was a big win for the Los Angeles biotech community and Agensys grew from 120 employees, with 50 PhD researchers, to over 300 employees.

A A decade later, after Astellas decided to relocate its operations in Santa Monica to Chicago, we convinced Gilead Sciences to acquire the Agensys facilities, widening a top-10 biotech company's stake in the Los Angeles life sciences ecosystem. It really put us on the map.

- A** In 2004, we also founded another biotech start-up, Cougar Biotechnology. At Cougar, we developed a novel small molecule, Zytiga (abiraterone) a potent drug for castration-resistant prostate cancer. We located the company literally across the street from UCLA Medical Center. At the same time, right next door to my own lab at the Jonsson Comprehensive Cancer Center, Professors Charles Sawyer and Michael Jung were actively engaged in collaborative research on prostate cancer that produced much of the discovery work on what became Pfizer's drug Xtandi (enzalutamide), a blockbuster for which UCLA continues to receive royalties to this day. Cougar was acquired by J&J in 2009 to gain access to abiraterone, which was subsequently approved as Zytiga by the FDA in 2011. Zytiga earned J&J US sales of \$3bn in 2018.
- A** My UCLA roots were further reinforced when my faculty colleagues Owen Witte, Jim Economou and Antoni Ribas joined me in starting yet another new company focused on engineered cell therapy. Kite Pharma was launched across the street from the UCLA Medical Center in 2009 and only later did it move to Santa Monica. Our mission at Kite, quite ambitious at the time, was to develop the first engineered cancer immunotherapy company around the autologous chimeric antigen receptor T-cell (CAR-T) platform. It was a dream that we were able to turn into a reality for patients. We developed Yescarta (axicabtagene ciloleucel), the first autologous CAR-T therapy to be approved by the FDA for non-Hodgkin lymphoma (NHL).
- A** By the time we sold Kite to Gilead Sciences in 2017 for \$11.9bn in the largest pre-commercial biopharma acquisition to date, we had 800 employees and a local good manufacturing practices (GMP)-certified commercial manufacturing plant scaled for the imminent approval of Yescarta. Under the new management at Gilead, Kite's workforce has more than doubled, to 1,850 employees, located in Santa Monica and in El Segundo, the site of a manufacturing plant that oversees the customized biology required to deliver Yescarta to each individual patient.
- A** That Yescarta is made here is another sign that Los Angeles has come into its own as a leader in biotech, combining top academic talent and business know-how to produce world-class medicines that advance patient care. The opportunities that came from my academic connections to UCLA have instilled in me a deep confidence in the city's future as a bench-to-bedside powerhouse in medical innovation.
- A** My newest and most ambitious project is Allogene Therapeutics. This company is pursuing an off-the-shelf CAR-T therapy against cancer. I am joined in this project by another colleague and former UCLA professor, David Chang, who has moved from heading Kite's R&D program to his new post as Allogene's president and CEO. For now, we are based in South San Francisco due to our history with Pfizer, from whom we acquired the asset. I am keeping my roots here in southern California by taking the lead in opening a new office in Los Angeles for Vida Ventures, a Boston-based boutique VC I co-founded and helped launch in 2017 with more than \$350m to support emerging and breakthrough science. We will work with other geographically focused VCs, including Westlake Village BioPartners, which is also here today, to provide hands-on expertise with a focus on start-ups that are making the Los Angeles metropolitan region their preferred home base.
- A** You see that all of us here today are deeply interconnected in pursuit of the same goal. I am interested in hearing from the others on the panel.
- A** **David Reese, executive vice president R&D, Amgen:** I am a refutation of the notion that Los Angeles is a transient place where people don't put down roots. I came to Los Angeles 30 years ago as a newlywed and except for a brief period on the faculty of the University of California, San Francisco, I've been here ever since. Both of us were looking for a place where I could do my post-med school residency and my wife could apply her new degree from Stanford Business School.
- A** Like for Arie, UCLA proved to be an attractive place for me to start a career in science and research. I ended up doing my medical training at UCLA's old Center for the Health Sciences campus just across the street from here. I was the chief resident in internal medicine when the 1994 Northridge earthquake hit nearby, which gave me my first exposure to crisis management. It was also during my first week as a UCLA physician intern that I met Professor Dennis Slamon, a mentor whose lab did much of the basic research on the HER2/neu oncogene that eventually produced the breakthrough drug Herceptin for breast cancer. I ended up spending a decade in Slamon's group, and later I ran a clinical research network with him.
- A** In 2005, I joined Amgen's R&D program, where I have held various roles leading up to my present position as the company's head of global R&D. To me, it was a natural transition from academic discovery to commercial development. The Los Angeles ecosystem proved fortuitous in offering me the best of both worlds. That critical mass is expanding and helps explain why I believe the area has much more to contribute in seeding innovations that work for patients.
- A** **Amir Nalberg, president and CEO, UCLA Technology Development Group:** I am a relative newcomer to the region. I arrived three years ago after serving as CEO at Yeda R&D Ltd., the commercial arm of the Weizmann Institute of Science in Israel. The opportunity came because UCLA had made a strategic decision to take better advantage of the commercial development opportunities from the research taking place in its labs. The bottom line is UCLA wanted to recruit someone who was familiar with cutting-edge academic science and could build and run a technology group more like a business. On a visit to Israel, representatives of the UCLA search committee invited me to breakfast, and four months later I, my wife and three children landed in Los Angeles.
- A** The commitment I find here to excellence in life sciences research makes my mission largely self-evident – it requires no explanation. Everyone understands the potential the university's vast talent base has on innovations that create significant downstream economic opportunities while delivering real value to patients. The Los Angeles region has not been an easy sell, so we must work hard to establish ourselves as a significant hub. Medical innovation is a global pursuit, where the winners will be those who are most effective in creating an ecosystem that can support their scientific assets and resources.

- A Mike Jung, university professor of chemistry and biochemistry, UCLA :** I've spent almost my entire professional life here in Los Angeles – 45 years to date. I arrived in 1974 after receiving my PhD from Columbia University and a post-doctoral residency at the Swiss Federal Institute of Technology in Zurich. It was simple: UCLA said it wanted me to come to Los Angeles and made me an offer. I took it. I grew up in the raucous French Quarter of New Orleans and Los Angeles presented as culturally a bit crazy too – ever since, I've enjoyed the city and enjoyed the work. Over the years I received numerous offers to leave UCLA and significantly increase my income. But happiness can't be bought. And I truly have been happy here.
- A Steve Rosen, provost and chief scientific officer, City of Hope National Medical Center:** I was trained as a medical oncologist with a background in lab work. I grew up in New York, graduated from Northwestern University's medical school honors program and, like Arie Beldegrun, did post-doctoral work at the National Cancer Institute – also as a member of Dr. Steve Rosenberg's lab, doing some of the important early work on cancer immunology. After that, I spent 25 years at Northwestern University, running its cancer research, trials and treatment programs. During that time, three of my four children, as well as my parents and sister, had relocated to southern California for the educational opportunities and the great climate, so when City of Hope approached me for a new position I decided to take a look. I quickly fell in love with the “succeed by doing well for others” culture of this institution and the commitment to research that benefits patients in fighting difficult, hard-to-treat diseases like cancer.
- A** Since I joined City of Hope a little more than five years ago, I've been heartened by the resources I've been given to build on this great reputation. My initial assignment was to bolster the foundational research program at our Beckman Research Institute, investigating the biology, chemistry and pathology of cancer and diabetes. Today, my role as provost and chief science officer consists of administering all City of Hope research programs, from basic and translational science to clinical trials, most of which center on cancer but also include a diversity of conditions, from diabetes to HIV. The many personal connections I've made – and the common links I share with the other panelists here today – reinforce my view that Los Angeles has the abundance of human capital required to keep generating the best new ideas in medicine.
- A Beth Seidenberg, managing partner, Westlake Village BioPartners:** I began my career on the East Coast but moved to Amgen some 20 years ago, where I served as the company's chief medical officer and head of global development. I exemplify a common theme, moving out to California with some trepidation, then falling in love with the geography, climate and a unique way of living that is very different than other parts of the country. After Amgen, I joined the VC Kleiner-Perkins in the Bay Area where I spent 14 years and, as a general partner, helped fund the growth of 15 successful biotech companies.
- A** All that time I kept my home in Westlake Village near Amgen's HQ in Thousand Oaks. The irony was I was living in the LA area even though my work involved investing in companies around San Francisco and Boston. I found it amusing that, considering my own weekly commute, colleagues at Kleiner-Perkins would talk about LA as another planet – too far away to spend any time there. My consumer tech counterparts took the same view until Snapchat took off and created a new geographic hot zone called Silicon Beach in the Venice area. Los Angeles promptly emerged on their radar screen.
- A** This is what is happening now in pharma and biotech. Finally, I happen to be living in the right place. I am now helping shape the future of the city after founding last September a new VC enterprise, Westlake Village BioPartners, jointly with Amgen's longtime head of R&D and a close friend, Sean Harper. We've raised \$320m so far. Our business mission is to seed the Los Angeles area's potential in life sciences, focusing on early-stage incubator companies with interesting novel technologies as well as a few later-stage plays that together will create a diversified portfolio marked by great science – and treatments that, while they might be developed here, will work for all patients, regardless of geography.
- A Peter Moglia, co-CEO and co-chief investment officer, Alexandria Real Estate Equities Inc.:** I am a UCLA graduate, which makes me an optimist about Los Angeles. I started at Alexandria in 1998. One of the first things our company founder Joel Marcus asked me to do was establish a biotech “cluster” in Los Angeles. I went and found an old warehouse in Pasadena where we are based and retrofitted it for lab space. We called it an Innovation Center, with a focus on early-stage companies, given that Los Angeles was then a nascent market for life sciences.
- A** We were able to lease it out fairly quickly, but soon found that these early-stagers would leave after two or three years – not just from our facility but from the Los Angeles area entirely. The reason was either they were getting investments from outside the region and their investors wanted them to move closer to where the capital was; or they had needs that were locally scarce, usually management talent. It was also true our business model focuses on “class A” facilities that are great for a company's image for recruiting and retention purposes but carry a premium that didn't fit local early-stage company budgets – at the time, their funding sources were “friends and family” contacts that did not value image as much as professional investors do. All this is starting to change and Alexandria is cautiously re-engaging in the market. The optimism has always been there and now it's starting to prove out.
- A Ken Schultz, chair and CEO, Trethera Inc.:** I wasn't born in southern California but got here as quickly as I could. Following practice as a physician plus five years as McKinsey & Co. in Europe, I arrived in Los Angeles to support Medtronic's artificial pancreas system for diabetes, which won Time Magazine's 2014 Invention of the Year. Later, I co-located to the San Diego area to lead strategy, innovation and business development for Halozyme Therapeutics. Having served during that time as an active board member for Trethera, the directors recruited me last year for the CEO role as well. Trethera is a start-up whose origins link back to UCLA's work in small-molecule DNA synthesis and repair space. Our lead candidate, TRE-515, is a first-in-class inhibitor of the enzyme deoxycytidine kinase (dCK). Today's fellow panelist Mike Jung, along with Dr. Owen Witte of the UCLA Geffen Medical School as well as several other prominent UCLA faculty, developed TRE-515 for use against solid and hematologic tumors.

A From my experience around the globe, the biggest value-added I see in Los Angeles is the access to early-stage start-up funding – though late-stage funding is not nearly as robust. We've raised well over \$15m for Trethera locally, with many of our investors coming from outside the industry. Having the entertainment industry as one of your shareholders adds a unique wrinkle – where else can a start-up claim that one of its principal investors is the screen writer for the iconic movie Toy Story? Los Angeles also has the unrivaled physical presence of many major academic research institutions, including, in addition to UCLA, Cal Tech; the University of Southern California, including its new Ellison Institute for Transformative Medicine; LA BioMed Medical Research Lab; the seven Claremont Colleges; and several others.

To Prosper, Stay Close

q As a group, do you believe the autonomous capacity to access, transfer and interpret large volumes of information has made geography irrelevant to success in today's research enterprise?

A Jung: The Internet has certainly democratized the way we scientists exchange information. But direct human interaction is unpredictable, which is precisely why it can be so useful to the pursuit of innovation. Closeness does count, especially when you have a burning question and can simply walk over to a neighbor's lab to find an answer.

A Reese: Technology gives us the opportunity to pursue collaborations remotely in a way that was not possible in the past. But we primates are wired to be social. Having intellectual capital massed together should never be discounted.

A Seldenberg: The common thread is that it's always hard to start a new business – but harder still to contemplate doing that from afar, separated from the researchers who develop the science and understand the condition as experienced by the patient. It is true that you can import the intellectual property from virtually anywhere. But if you want to build a viable commercial business, a supportive surrounding ecosystem of other like-minded businesses as well as a familiarity with the stakeholders responsible for shaping local practice and regulation is extremely important. I've experienced this dynamic at work before in Boston; in Los Angeles the same thing is happening now, but at a more rapid pace.

A Beldeggrun: I am finding our investors – including Gilead Sciences, in the case of Kite – are increasingly willing to come and work where the expertise lives. Many of Gilead's management team responsible for the Kite acquisition are now sitting in Santa Monica. I think this trend will continue.

A Reese: Looking at the future of this industry writ large, the engine of growth is the mixing of diverse platforms, technologies and talent. Multidisciplinary expertise is the entry point to all the new science, such as the “omics” field, which requires such diversity if we are to understand the roles, relationships and actions of the various molecules that populate the cells of an organism. Hence it is simply good judgment to stay close to where this research is being conducted – the pace of learning is extraordinary and cannot be evaluated from afar.

LA's Assets

q What's attractive about the Los Angeles biotech landscape today? Are we at an inflection point in terms of the sector's growth prospects?

A Beldeggrun: We are excelling at advanced gene and cell-based technologies that take us beyond the pill. When we sold Cougar to J&J, it was because we made a pill – it was very easy for J&J to integrate that modality to its base operations in New Jersey. It is not as easy for Gilead to relocate the manufacturing of the autologous CAR-T technology behind Yescarta. As its use by patients grows, our original \$500m investment in the complex, customized re-engineering of individual cells will stay here because of the expertise this region has in this high-touch production.

A The FDA is sending staff out here to understand the process of re-engineering the human immune system to deliver a treatment to patients. There are multiple, small start-ups founded by bioengineers, lab specialists and CROs (contract research organizations) all interested in being first with the next generation of medicines targeting the human immune system. It started with the low hanging fruit in cancer but is expanding beyond that to the autoimmune disorders and inflammation affecting millions of people in the US and worldwide. Such expertise is not easily replicated and transferable in the same way as can be done with a small-molecule pill.

A Reese: I am biased because Amgen already has the best genetics database in the world due to our investment in Iceland's deCODE genetics project. We now have millions of participants enrolled from around the world. We have another project underway with a Colorado-based biotech, SomaLogic Inc., to investigate how proteins impact health status and disease progression in the human body – it's the largest, most comprehensive proteomics experiment conducted to date.

A What's driving us is the necessity to attack disease in a different way than traditional methods, where we can learn to generate new insights about targets and pathways against the hardest problems in medicine, like protein degradation or eliminating the blood-brain barrier. At present, only about 15% of the human genome is druggable. We have to push the technology boundaries to make tractable disease targets that are currently out of reach.

A Expertise from many parts of the scientific community, from chemistry to biology to physics and engineering, will be necessary to solve these challenges. I am optimistic on what we can achieve collectively – and the university infrastructure we have cited as a feature of the Los Angeles biopharma ecosystem gives us that in spades. The molecular and cellular engineering capabilities that exist right here give this region a big edge in translating theory into

therapy that works for patients. We have the opportunity here to put all this together.

A Seidenberg: In terms of inflection point, what set things afire in the Massachusetts hub was the decision by Novartis 16 years ago to move its major global R&D operation to Cambridge from Basel, under the high-profile leadership of cardiologist Mark Fishman. That was the “big bang” that made Cambridge a destination for other big pharma and in turn drew in a host of satellite smaller biotechs. Gilead Science's acquisition of Kite Pharma in 2017 as well as its expanded research commitment to southern California has had a similar, if smaller impact compared with Novartis. If over the next couple of years we get some additional local investments by Amgen while simultaneously attracting a new big pharma player to relocate key R&D operations to Los Angeles, then it's game over. We are already repairing the deficit in venture capital with the formation of Westlake Village BioPartners as well as Arie Belldgrun's Vida Ventures, which will give us the concentration of capital assets that has been lacking to date.

A Nalberg: I'd emphasize the enormous extra lift provided by our local academic institutions and teaching hospitals. There is a significant follow-on effect in the amount of funding this area gets from the federal research agencies like the NIH and the National Cancer Institute (NCI). Los Angeles-based research institutions received \$1.1bn in NIH funding in 2018, the largest amount of any county in California. Two of the top-five grant recipients from the state were based here: UCLA and the University of Southern California (USC).

A Seidenberg: Yes. Academic relationships are a factor in our favor – so much so that few people realize that the biggest challenge facing Los Angeles biotech is the chronic shortage of private laboratory real estate. It's not seen as an issue because of all these university-based assets. It's tough getting outsiders to invest. Hence start-ups like Atara Biotherapeutics, another allogeneic T-cell immunotherapy company where I serve on the board of directors, must invest and build such facilities on their own. With help from the city of Thousand Oaks, Atara recently opened a state-of-the-art allogeneic T-cell operations and manufacturing center near the Amgen HQ.

A Belldgrun: Let me add some additional context – we are all here today to participate in UCLA's second annual Bioscience Innovation Day. The first one last year attracted about 450 people from southern California and around the country. This year I'm told the number has nearly doubled. A few months ago I participated in a similar daylong life sciences event hosted at Research Triangle Park in North Carolina, which drew about 900 attendees. I was impressed and asked my hosts how long they've been doing this meeting – the answer was 30 years! I took from that brief exchange that our prospects going forward are exceedingly bright. Today, we have a lot of the top people from companies, research institutions and VCs throughout the country. Next year, they will bring their teams with them too. People will have figured out what great things are going on out here – and they will be ready to do business. And it has happened in just two years, compared with three decades.

A Reese: Another favorable trend is the market for scientists and researchers is very strong. The recruitment field is highly competitive. Amgen is not experiencing any down cycle in wage expectations of the people who come here.

A Jung: David is right. The young people we hire today are getting offers from everywhere. No one feels compelled to stick to one track in academia and ignore the possibilities that can come from partnering and entrepreneurship. Arie is a prime example of those possibilities and what can be achieved in applying a medical or science background to build a great enterprise.

A Belldgrun: Most biopharma scientists in academia today are highly opportunistic and this has rebounded in favor of Los Angeles due to its top-rank institutional assets. No one is in an ivory tower or giving anything away. My friend Mike Jung is not the man I knew 20 years ago. He's not only a distinguished scholar – he's a savvy and successful businessman.

q How strong is the CRO and contract development and manufacturing organization (CDMO) presence in Los Angeles?

A Seidenberg: It's a key variable that will take a bit more time to develop. Cell and gene therapy, including gene editing, are going to compose the major source of therapeutic opportunities in the next decade. Right now, there is no truly robust capability in the contract research world to meet the production challenges around these complex, highly personalized therapies. The result is that developer companies like Kite (now Gilead) are doing it themselves. They are building their own facilities. There are also the companies like Allogene, which are working on allogeneic standardized, off-the-shelf approaches to cell/gene therapy rather than the prevailing autologous one-off model, a trend that offers a less cumbersome and possibly cheaper way to deliver treatment.

A The point is we now have at least one big pharma in Los Angeles expert at this type of manufacturing. From that base many CDMOs will start to form around it. The precedent is Genentech and how its leadership in production of monoclonal antibodies spurred the growth of multiple new suppliers of this technology in the Bay Area. It's entrepreneurial metastasis – and I expect Los Angeles will come into its own as a national locus for expertise in cell and gene-based manufacturing. Like VC capital, it's another key element to add to the biopharma ecosystem now coming to life in Los Angeles.

Mind The Gaps

q What are the challenges – the gaps that must be addressed to bolster Los Angeles' credentials as a world-class biotech hub?

A Schultz: One thing I am not sure we can tick the box on is access to venture capital. Funding for the early stage is there – my own company secured non-VC money right at the start – but at the crucial later stages when the challenge is funding proof-of-concept trials, local investors seem more reluctant. I don't see as many of the globally integrated VCs opening branch offices in Los Angeles and I noticed a recent \$40m VC deal with City of Hope that made the

investment contingent on re-locating the company to Cambridge, MA. A 2019 Boston Consulting Group (BCG) report, *Stars Aligned*, showed late-stage VC funding in southern California trailed the Bay Area by over 90%. I guess my question is, as a new biotech entrepreneur, I'd like to tick that box – but are we there yet?

A Seidenberg: There is a distinction at work here. An early-stage investor will want to be involved in the details of building the enterprise from the ground up, vetting and monitoring your business plan to make the right decisions on physical plant and talent recruitment. There is an incentive to stay local. At the later stage, VC money can enter from anywhere because the basics of the business and its value proposition are already in place and it's easier to insist on a translocation contingency as part of the deal. That's just the reality. Our mission at Westlake Village BioPartners is to get actively involved and build the start-ups we invest in right here in Los Angeles. And we also want to bring in late-stage money, as we have done for Atara Biotherapeutics and as Arie Beldegrun did for Kite Pharma. Getting that funding is not going to be an issue if the fundamentals are right.

A Jung: Lab space is a pressing issue. I can see from my perspective that space is really hard to come by off campus. I understand that Alexandria Real Estate Equities has bought land in Culver City and is going to build there. We aren't going to fulfill our potential in cell and gene therapy unless we add to our lab infrastructure in Los Angeles.

A Seidenberg: Having to wait in line for lab space is a key concern for start-ups. Any downtime that affects your development progress costs money. The clock is always ticking on the intellectual property.

A Schultz: At more than 4,000 square miles, Los Angeles county is bigger than Rhode Island and Delaware combined. We have no center of gravity in terms of real estate; instead we have clusters of lab and incubator facilities in Pasadena and adjacent to Amgen in Thousand Oaks. Rather than a singular geographic blob, the biotech industry here will look more like scattered droplets where scientists and teams can work closely to one another.

A Seidenberg: It's not going to be possible for Los Angeles to look like Kendall Square in Cambridge. We are likely to grow out to resemble the Bay Area, with many pockets or clusters of activity and a big divide between the peninsula and East Bay where you have people who just won't shuttle back and forth on the bridges. It hasn't hurt Silicon Valley too much – the big problems up there are housing costs, regulation and the war for talent leading to a challenge in recruiting and retaining top-quality researchers and experienced staff.

q What about enlightened public policies focused on zoning and tax breaks for incubators and a better overall approach to land use, including incentives for affordable housing? Does government actually work in California?

A Seidenberg: Where I am based, in the Thousand Oaks area, the response of city councils and other local government has been tremendous. Restrictive zoning there is not an issue. There has actually been a shift in emphasis over the past few years from attracting investment in warehousing, retail and manufacturing to biotech and other high-tech sectors that leave a small footprint on the land and offer high-paying jobs. Jobs data assembled by the industry have had a big impact in showing that life sciences generates more tax revenue than most other sectors and has a big spillover impact on retail and other businesses that depend on high-income workers.

A Moglia: One of the big challenges in Los Angeles is zoning laws. There is very little land that is authorized for R&D activities; if you read the zoning code it is hard to determine whether or not a wet lab is even allowed here. We've discussed this with the city and it is looking at clarifying the legal situation. More flexibility on zoning and land use is definitely a plus given the demand for space to conduct research.

q We should conclude with a consensus on the next steps necessary for Los Angeles to realize its potential in assembling the science, capital and talent to deliver tomorrow's medical breakthroughs. As key players representing a cross-section of the city's current biopharma infrastructure, how can you leverage this geography of opportunity to become top finisher in the global race for the knowledge assets that treat and cure disease?

A Seidenberg: On the practical side, the biggest thing that must be fixed is the real estate. We need more lab space and a strategy on where to place it to achieve the greatest synergies between industry, services and adjacent businesses, academia and the big teaching hospitals. We're solving the funding issue. With the opening of the Vida Ventures office, you are seeing other VCs following the same geo-centric path as Sean Harper and I have done. As far as late-stage money is concerned, that will come once we build more quality companies here with reputations in the new sciences.

A A larger issue is changing the cultural mind-set, by tackling up-front the myths that others in biopharma seem to have about Los Angeles. For example, I still hear from outsiders that it's hard to recruit talent. That's the mantra. I just smile and try to ignore it. It might have been true once – when Sean and I started at Amgen 20 years ago, we were just ourselves; there was no team. But that proved to be an advantage. David Reese joined us from UCLA because, as he said, it was an opportunity to build something. The same bootstraps mentality also appealed to Kite's eventual co-founder, David Chang, when we first reached out to him.

A There are so many other examples of successful people who wanted to be part of this culture of individual initiative and trying things differently than what was commonplace back east. We must put out the message that Los Angeles is small and big at the same time, with strengths and gaps that make it a wonderful place to reinvent yourself – and to keep doing it. I'd also mention that Los Angeles has an abundance of research talent in other technology sectors. This will be increasingly important as medicine becomes more personalized, using platforms that deliver treatment in ways no longer reliant on the small-molecule pill. We also shouldn't forget those service functions like legal, accounting and finance that every new start-up needs to grow as an enterprise. These are all here at scale.

- A Schultz:** I agree that we have a lot of R&D talent. What are not so prevalent are people with general management expertise along with practitioners in specialty functions like CMC (chemistry, manufacturing and controls) and regulatory. We also need to seed that class of entrepreneurs who have built companies and closed them down – numerous times. This is an important and hard-won source of wisdom about how biotech really works.
- A Naiberg:** UCLA is committed to establishing a closer connection between academia and industry. We feel it has to be integral to any growth agenda for biopharma in Los Angeles because the architecture is so rich in potential. Our Technology Development Group relies heavily on mentoring work. For example, we work with many of you here in this room as external experts to judge and support projects initiated by our faculty that can lead to successful commercialization.
- A** The degree of commitment and involvement by industry colleagues has gotten deeper with time. They are mentoring our teams every step of the way, creating those milestones that keep everyone focused on realizing an investment return from all the new science our faculty creates in the lab. What we've achieved together in the two and a half years since I arrived at UCLA is gratifying. The model deserves to be replicated throughout the region as a priority for the entire research community.
- A Beldegrun:** My wife sits on the board of directors at Cal Tech. I understand an investment fund is being created to support more foundational work there on biotechnology. The point is Cal Tech wants to increase its footprint in the new science.
- A Rosen:** I share Amir's perspective. City of Hope is an engine of productivity when it comes to developing new therapeutics. Of late, we've had two projects licensed out that amount to a vote of confidence in the several hundred million dollars we spend annually on research. Since I arrived five years ago, we've recruited about 70 new lab investigators; more than half of them came from tenured faculty positions. Also, City of Hope does not offer tenure. It's a major vote of confidence in our ability to make new discoveries and bring them to start-up. Our board of directors has endorsed us setting up a separate biotech business development office. As a result, I expect the breadth and quality of these relationships to increase.
- A Beldegrun:** Another area we can agree on is tax policy and incentives. Many parts of the country now offer tax breaks in return for investing in a state or community. When Massachusetts started doing this, you began to see more companies opening facilities in the state. The latest is France's second-largest drugmaker, Servier Group, which opened a new US HQ in Boston earlier this month.
- A** California is a state that has never, to my knowledge, offered tax breaks to biopharma in return for investments or jobs. It may be appropriate to discuss with the city and county how they intend to keep us as a leader in biopharma innovation. Mark Ridley-Thomas is the county supervisor who represents the area around UCLA. His record in support of the biotech sector has been unwavering. What's unclear is the position of the city council and the Los Angeles delegation in the state legislature.
- A** In the end, we know that if Los Angeles is able to attract another big pharma to locate here, in addition to Amgen and Gilead, it would be a game changer – further entrenching us on the map in ways that could attract more mid-size or smaller biotechs to invest and add to our base in human capital. I'd also like to ask my friends at Amgen if or how it plans to spend the \$30bn in cash it reported having on hand at the JP Morgan investor conference in January. My hope is that a good portion of it will be put into projects here.

A 'Big Bang' – And The Olympics Wild Card

- A Schultz:** What we're talking about is a "big bang" event – bigger than the \$12bn Gilead Sciences paid for local innovator Kite Pharma two years ago.
- A Beldegrun:** That's why it's doubly important to engage Amgen CEO Bob Bradway and new Gilead Sciences CEO Daniel O'Day as ambassadors to the rest of the big pharma community in making the case for high-level investments, as they have done in Los Angeles.
- q** UCLA's Technology Development Group will be holding its third Biosciences Innovation Day a year from now, at the start of a new decade. Do you have a sense of what the theme will be? What next are you excited about?
- A Naiberg:** Next year, we will focus on the who, why, when and how of partnering. This year, this activity was a sidebar. The sentiment among attendees I spoke to is partnering has to be front and center. That includes active participation not just by the UCLA community but by other institutions in Los Angeles county – anyone who wants to join us. Our goal is to make the annual Biosciences Innovation Day a one-stop shop for showcasing biopharma innovation to highlight and advance best practices. And of course we are looking to increase turnout, which this year vastly exceeded our expectations.
- q** Finally, Los Angeles has received the nod to host the summer Olympics in 2028. Among other things, preparations for this global, high-profile event usually entail significant local investment in infrastructure as well as a "rebranding" of the host city's image. Is there an opportunity to include biotech and the life sciences in these initiatives?

A Reese: All big companies and employers in the region are likely to benefit from the media spotlight that will be placed on Los Angeles and its incredible diversity of people and talent. If it leads to the build-out of a public transit infrastructure, that will help expand the cluster-based work and lifestyle approaches that many young scientists seem to prefer these days. We need to maintain our focus in being attractive to this employment demographic.

A Beldegrun: There is no need for any elaborate effort to rebrand what we do. My life in Los Angeles tags me as an inveterate optimist. It's simple: Los Angeles – The Next Biotech Hub.