

Here To Stay: Inception Sciences Shows Why Build-To-Buy Works

By Marc Wortman (Contributor)

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Executive Summary

Born at a time when venture capital found few exit opportunities for early-stage companies, build-to-buy helped mitigate the risk in investing in uncharted science. But the model is flourishing even in this period of wider capital options.

- The build-to-buy strategy partners venture-financed start-ups with pharma companies holding options to acquire the firms at preset valuations and milestone-based exit points.
- Several venture funds and venture incubators now align company creation with the needs of pharma partners, often with exclusive options to buy the biotech.
- Versant pioneered the build-to-buy approach with Inception Sciences, which has recently spawned a sixth company and third R&D site, showing that both venture capital and pharma continue to value the de-risking strategy for early-stage innovation.
- While mitigating investor risk, the pre-negotiated deal terms cap returns, reducing chances for greater gains traditional venture models might reap in biotech boom times, but the sale to Celgene of Quanticel, Versant's first true build-to-buy, shows how a consummated option deal can work brilliantly for both pharma and venture capital.

Necessity mothered the build-to-buy strategy. Some thought good times might kill it. At a time when venture capital found few exit opportunities for early-stage companies, build-to-buy helped mitigate the risk in investing in uncharted science. In better biotech financing times, though, the need for closing off other exit options might seem to have gone away. Yet if anything, build-to-buy dealmaking has accelerated as the interests of venture capital and pharma move into ever closer alignment.

Structured acquisition deals or purpose-built biotechs – other names for build-to-buy – are typically created by venture funds in partnership with pharma companies. The pharma takes an exclusive option to acquire the business at a previously agreed upon price triggered by achievement of specific milestones, such as development of a clinic-ready asset. In return for the exclusive option, the pharma generally holds no equity in the company prior to its purchase but agrees to support R&D costs for the life of the company. If the partner elects not to purchase the company at the designated milestone, all rights revert to the owners.

For the pharma partner, the build-to-buy deal offers another way to access early-stage innovation and venture creation without having to devote internal R&D capabilities to high-risk programs. At the same time, the deals provide some tax advantages by keeping R&D spending off P&L books, cap the eventual

deal price, and keep clear who owns what intellectual property in development. The deals control costs within a tightly directed, highly capital-efficient set-up.

For investors the deals lower their risk by aligning their investment in uncharted science with the known needs of a potential acquirer from the start. Significant for such high-risk investments, typically the VC controls a greater percentage of the company equity than traditional syndicated financings, increasing the total return on a consummated sale even if the deal terms cap the sale price. The scientific goals are clear, business handoffs clean. In the end, scientists and bean counters alike can find much to like about the deals.

But in today's less risk-averse capital markets, the capped upside might seem outmoded, no longer necessary for investors willing to sustain a company for the long haul and eager to maximize returns with an outsized public offering or M&A exit. In fact, some blue chip venture funds have not done build-to-buy deals to date, such as F-Prime Capital (formerly Fidelity Biosciences). Entrepreneurs also might feel uncomfortable seeing their technology and efforts narrowed to a single partner-pharma's specific needs. At the same time, some pharmas, among them **Sanofi**, have not jumped on the build-to-buy bandwagon, sticking to corporate strategic venture investing as a way to get close to emerging biotechs.

However, a slew of newly launched build-to-buy biotechs and recent closings of at least four new funds dedicated to some degree to aligning venture start-ups tightly to a pre-contracted pharma buyer indicate that good times have not dampened venture investors' need to hedge their bets nor pharmas' willingness to pursue early-stage opportunities in concert with VCs. (See *Exhibit 1*.) Build-to-buy is proving to be an early-stage biotech business model for all seasons.

Exhibit 1

Build-To-Buy Flourishes

VC, Fund Amount, Closing Date	Pharmaceutical Partners	Select Purpose-Built Companies and Partner
Atlas Venture, \$280m, April 2015	Novartis and Amgen	Spero and Roche; Ataxion, Rodin and Biogen Idec; Annovation and The Medicines Co.; Quartet and Merck
Avalon and GlaxoSmithKline provide \$10m in Series A funding, with up to \$465m from GSK	GlaxoSmithKline and COI Pharmaceuticals	Iron Horse Therapeutics, Sitari Pharma, Silarus Therapeutics, Thyritope Biosciences, Adrenergics, Cadherx Therapeutics, Calporta Therapeutics and GSK
Flagship Ventures, \$537m, May 2015	AstraZeneca, Nestlé Health Science and Bayer CropScience	Undisclosed
MPM Capital, \$400m, May 2015	Novartis and Astellas	Semma Therapeutics and Novartis; Potenza Therapeutics and Astellas
Versant Ventures, \$305m, Dec. 2014	Multiple and Inception Sciences	Quanticel and Celgene; Inception IBD and Celgene; Inception 3 and 5 and Roche

Company reports; Strategic Transactions

Aligning Start-Ups With Pharma

Over the past five years VCs have moved sharply to align company-creation with the needs of potential acquirers. When Atlas Venture closed its Atlas X \$280 million biotech fund in April 2015 with **Novartis AG** and **Amgen Inc.** as limited partners, Atlas partner Bruce Booth noted that the LPs will enjoy “strategic proximity” to start-up formation, some of which will result in exclusive options for companies or assets.

Booth pointed out in a 2013 blog post [\[link\]](#), “Today, over 75% of our deals have corporate venture groups as co-investment partners; this number was below 5% a decade ago.” With early scientific discussion between the venture incubator and pharma leading to preset goals even before a company launches followed by joint oversight committees and frequent communication between scientific teams, build-to-buy binds a biotech’s R&D more directly to pharma’s needs than any other start-up venture model.

Versant Ventures pioneered the systematic approach to the build-to-buy model when it set up **Inception Sciences Inc.** in 2011 to incubate and then operate a steady stream of build-to-buy companies. Versant’s experience with Inception shows how an early stage-investing model forged in adversity became a venture capital fixture.

Build-to-buy began in the aftermath of the financial crisis when early-stage biopharma venture investing had fallen badly out of favor. Hard-pressed to recoup their limited partners’ money, many VCs shied away from the risks and long time lines associated with unproved technologies and early-stage assets. With venture capital drying up, biotechs could not advance many promising discoveries. Only M&A remained open as an exit, and even that was a risky bet for investors because pharma’s pipeline needs didn’t necessarily align with a biotech’s R&D efforts or the level of investment going into companies. Yet pharma’s need for innovation remained a constant.

Jerel Davis, PhD, joined Versant as a partner in 2011. He recalls that at the time Versant noted that pharma never lost its hunger for innovation. “Exit paths cycle,” he says, “but year after year, we saw that there were consistently about \$20 billion in pharmaceutical acquisitions” of biotechs. Versant managing director Bradley Bolzon, PhD, wanted to create a risk-mitigating investment vehicle appetizing enough to get pharma to take a nibble earlier in the investment cycle.

Bolzon envisioned a strategy in which Versant would incubate and seed early-stage ventures, many of them based on technologies licensed out of academia, while bringing in potential pharma-partners virtually from the start. Versant incubated promising biotech ideas, pharma would tell Versant where their R&D interests lay, Versant would seed and then provide equity financing to launch the biotech to fulfill those needs, and, with locked-in terms for a pharma partner to buy the company, the pharma would then support R&D directly. The strategy gave investors the assurance they needed that success within carefully delineated parameters would eventually bring a payout. Given the pharma support for R&D, Versant could afford to finance most, if not all, of the equity component of the company or syndicate as needed, dramatically increasing its ownership stake while reducing its risk exposure. “This is a different risk-reward ratio than traditional venture,” Bolzon told *START-UP* at the time of its first build-to-buy deal.

(See “Quantice/Celgene: The Importance Of Linking A Financing And An Exit” — [START-UP](#), November 2011.)

Bolzon had a couple of precedents to look to in developing the model. In July 2011, with Versant as its largest shareholder, **Amira Pharmaceuticals Inc.** sold itself to **Bristol-Myers Squibb Co.** for \$325 million up front plus earn-outs. However, BMS didn’t want some of Amira’s assets, which Versant spun off into two separate LLCs, **Panmira Pharmaceuticals LLC** and **Flap LLC**. (See “BMS’ Purchase Of Amira: When An Acquisition Is Really An Asset Sale” — [START-UP](#), September 2011.) Effectively in the process of selling Amira, Versant had turned the company into an incubator for two wholly new biotechs – including one that served only as a holding company for an existing asset deal in place with **GlaxoSmithKline PLC**. [\[See Deal\]](#)

Around the same time that year, Versant launched [Quanticel Pharmaceuticals Inc.](#), with [Celgene Corp.](#) providing \$45 million in R&D support for development of Quanticel's tumor genomic analysis technology and related pipeline. Versant put about \$10 million into the company. If Quanticel progressed its R&D to the negotiated milestones, Celgene would buy the company outright at preset terms.

Amira's success and the promise of the Quanticel deal sparked Bolzon, Amira's board chair, and its chief scientist Peppi Prasit, PhD, to conceptualize a way to incubate similar deals in a systematic way. They drew up the idea for an R&D site that would both incubate new biotech ideas and operate the companies it spawned. A long time industry R&D veteran, Prasit became CEO of Inception Sciences. With wide scientific contacts, he set up R&D near the former Amira site in San Diego and later an additional lab in Vancouver.

The Quanticel deal covered the entire company, personnel and all, but Clare Ozawa, PhD, now Inception Sciences' chief operating officer, says, "Pharma typically is interested in acquiring drugs not people and infrastructure." So, she says, Versant sets up Inception business entities in a way that "keeps people separate from the company." The scientists work for the parent Inception Sciences. As such, says Davis: "They continue to be responsible for sourcing ideas for the pipeline" of new Inception business opportunities while they work on existing companies. He thinks that the model incentivizes scientists more than being part of a traditional biotech because they can participate simultaneously in different business opportunities, giving them "multiple shots on goal like a VC." He adds, "This is not a CRO. It's very far from a CRO."

There are now six Inception companies. (Including Quanticel, Versant has now done three build-to-buy deals independent of Inception.) Inception didn't get into creative naming. These biotechs were as purpose-built and impersonal as wings in a factory; the first five offspring were simply numbered in consecutive order. All five continue to operate. The inaugural [Inception 1 Inc.](#) focuses on a single target for fibrosis for partner [Shire PLC](#). According to Ozawa, Shire's option triggers upon successful delivery of a development candidate (ready to enter IND-enabling preclinical toxicology studies). Unlike its brethren, [Inception 2 Inc.](#) remains unpartnered while pursuing unidentified cancer targets and approaches. Versant's Davis insists, "In all cases, the Inception companies have to be ones we'd back on our own. We decided not to partner this one because we saw more upside than pharma saw."

[Inception 3 Inc.](#) was the first of two deals done with [Roche](#). The company focuses on developing new ways of treating hearing loss, "a tough area and relatively uncharted science," says Shafique Virani, MD, Roche's global head of neuroscience, ophthalmology and rare disease (NORD) partnering. "The program involves injecting drugs directly into the inner ear. The biology is very tricky. But so far the progress made has been really fantastic from our point of view." [\[See Deal\]](#)

In partnership with [Bayer Healthcare LLC](#), [Inception 4 Inc.](#) focuses on discovering new drugs for a novel target and pathway, for patients with eye diseases, such as wet age-related macular degeneration and geographic atrophy. [\[See Deal\]](#)

[Inception 5 Inc.](#), which Virani also oversees for Roche, began operations in June 2014, broadly looking into ways to remyelinate damaged neurons in multiple sclerosis (MS). Both 4 and 5's sales will take place at the IND-ready stage, whenever that comes. Each sale, according to Ozawa, has "no set time for a trigger. It is based on reaching the milestones." Virani concurs, "We let the science guide us." [\[See Deal\]](#)

The VC closed a \$305 million fund in December 2014 to help in part to support a new Montréal Inception site. CEO Prasit's earlier employment at Montréal's now shuttered Merck Frosst research center gave him contacts with many scientists available in the region. (See "[Versant Continues 'Build-To-Buy' With New Fund](#)" — *START-UP, December 2014*.) In December 2015, Versant announced that the site would be home to [Inception IBD Inc.](#), with Celgene supporting R&D and holding an exclusive option to acquire the company. The new biotech will pursue novel treatments and diagnostic biomarkers for irritable bowel disease using a proprietary mouse model for ulcerative colitis spun out of France's Inserm research center.

(See ["Versant Launches Inception IBD, A New Company With Old Roots" — START-UP, December 2015.](#)) Versant led a syndicate alongside Fonds de solidarité FTQ and Inserm Transfert Initiative (ITI) that funded the \$14.1 million Series A round. [\[See Deal\]](#) That is the third build-to-buy deal Versant has done with Celgene, which promised to provide \$45 million in support for IBD's R&D.

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– Clare Ozawa, PhD

A Cultural Shift For Pharma

According to Ozawa, each Inception deal is structured in a similar way and includes a collaboration agreement covering governance, a research agreement, an option agreement and an M&A agreement. “When we get to the trigger [for a sale],” she says, “there's no negotiation left. It's all worked out from the beginning.”

Virani negotiated much of the two deals on Roche's behalf and says that the deal for the first joint venture, Inception 3, took “almost two years to craft.” Part of that time was about the partners becoming comfortable with each other. “We handed off responsibilities for early-stage R&D,” he says. “That represented a cultural shift” for Roche at the time. He says that the most time-consuming part of the entire negotiation revolved around “what if the big pharma doesn't acquire the company.” In the end a great deal of know-how will have gone into the business and intellectual property will have resulted, some of which will almost certainly have value, sale or not. He says that both Inception Sciences and Roche retain freedom to operate in the biological space. “If Roche or Inception wants to pursue remyelination in Alzheimer's,” which is outside the scope of the Inception 5 MS program, “each has to be free to do that. We have specific language on who owns what IP. These are big issues that take big agreements, far bigger than standard licensing agreements.”

Obviously, Roche found the lengthy dealmaking process worthwhile. The pharma placed a large value in accessing emerging science in an area where it did not have existing capabilities and divesting some of the risk while still tapping some of the most innovative and enticing science in an area of high unmet need. “It gives us another tool for more dynamic portfolio management,” Virani says. “Part of the idea is to hand off work in a more nimble and biotech-like setting, while bringing in a top drug-hunting group. These are people who can crack the target and crack the chemistry.”

Still, he insists that pharma must have an upside for its participation. “It is fair to ask for terms that give an offset from current market valuations” for biotechs, Virani says. “We bring non-dilutive funding, R&D expertise and committee participation. The numbers have to make sense: build-to-buy has to cost less than doing it ourselves.”

Clearly, Roche has become comfortable with the build-to-buy deal because it has since done two more early-stage joint ventures unrelated to Versant or Inception. Roche entered into a partnership with the Atlas-incubated [Spero Therapeutics LLC](#) in April 2014. [\[See Deal\]](#) Roche is providing non-dilutive R&D funding to Spero, and will have the option to acquire Spero's anti-infectives program at the IND phase, at pre-negotiated terms including an up-front payment and milestones. (See ["Spero Therapeutics: Remodeling Antibiotics" — START-UP, December 2015.](#)) Roche also inked a co-development agreement in July 2014 with Montréal-based venture capital firm AmorChem LP, to work on disease-modifying small-molecule treatments for the rare genetic condition Steinert's disease, or myotonic muscular dystrophy. Virani says, “Inception's structure provided the basis” for both deals.

A Solution For Venture's “Math Problem”

Even in the presently relatively capital-rich times for biotech, VCs face an ongoing problem in making sufficient returns for their funds through traditional venture finance, especially with the jumbo-size funds recently raised. Atlas' Booth pointed out in a [December 18, 2015, blog post](#) that greater ownership is one solution to what he called the "Venture Capital Math Problem." He wrote, "If you only own 15% to 20% of your exits, getting to an attractive 3x+ overall fund return is very difficult, even in a bull market like the one we've been in. But having more than 40% ownership positions at an exit makes it very doable, as evidenced by some recent huge winners (e.g., Flagship owned 44% of Seres Therapeutics [[Seres Therapeutics Inc.](#)] and Third Rock Ventures owned 47% of SAGE Therapeutics [[SAGE Therapeutics Inc.](#)] after their IPOs)."

According to Ozawa, the Inception deals are modeled after [Quantical Pharmaceuticals Inc.](#), with Versant putting in about \$10 million and the partner supporting R&D with about \$45 million. Versant, Inception team members and academic founders have kept 100% of Inception company equity until Inception IBD. Alongside Versant, "the model," she says, "is also great for employees and founders as it limits VC dilution in ownership." For IBD, the VC saw strategic advantages in syndicating with Inserm's investment group to seed the company initially in France and in working with the regional Fonds de solidarité FTQ (which is also a limited partner in Versant's latest fund) in setting up the new site in Montréal.

In thinking about build-to-buy exits, Davis calls Quantical "a positive case study for VCs." In April 2015, Celgene exercised its acquisition rights, paying \$100 million up front for the biotech. The approximately 10x return for Versant does not include up to \$385 million in earn-outs based on R&D and regulatory progress. [[See Deal](#)] While no Inception company has sold to date, Davis and Ozawa both anticipate the first sale will come in 2016, though they won't say which company will be acquired.

Of course, structured acquisition deals exist because of the high risk that the programs will fail; not all deals by any means have a happy ending. For instance, Novartis walked away from its option to buy Proteon Therapeutics in 2014. [[See Deal](#)] Novartis had teamed up with Proteon's lead investor, MPM Capital, as part of an ongoing sidecar fund investment to procure rights to drug candidates after proof-of-concept is established. The JV has made multiple asset-centric investments, but Novartis turned down the chance to buy Proteon's form of a human enzyme called elastase, labeled PRT-201. The experimental drug was intended to help improve the outcome of a surgical procedure often used to prepare patients with kidney failure for hemodialysis, but a Phase II study missed on a secondary outcome. Reports indicated that the partners could not agree on deal terms to continue PRT-201's development. (Evidencing investors' belief in the drug, Proteon has since gone through both additional institutional rounds and a successful public offering.)

Hoping to prevent just such a JV-partner clash scenario at Inception, Ozawa claims, "We have worked out safeguards with the partners about who takes on the financial risks. It takes a lot of forward thinking and that's quite time-consuming."

Despite the capped upside and the vagaries that go with early-stage assets, Davis insists, "Build-to-buy businesses need to hold their own in multiples and IRR back to our funds. A great fund returns 3x capital to investors. Build-to-buy has to be accretive to our funds so terms have to take into account failure. We need to be well north of there to account for the risk we're taking." He says that the Quantical deal, born in tough times, shows, "There can be great returns [from build-to-buy deals] even in the best of market climates."