

BioCentury

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FINANCE

INVESTING UPSTREAM

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After a decade of focusing on public investments and later adding private investments to its remit, RA Capital is getting into the business of starting companies from whole cloth. The firm thinks having a dedicated financier from start to acquisition or profitability offers the continuity of support that many companies are seeking.

RA Capital isn't revealing many details about its initial two newcos, except to say the areas will include dermatology and Orphan diseases. Nevertheless the move will put the firm in a rare position of being a single institution that participates in the entire financing spectrum from formation to investing in well-established public companies.

"You have a single cohesive team pulling in a single direction, with maximal flexibility to invest in wherever the science and the value take us," said the firm's Peter Kolchinsky. "Science doesn't care about whether you're public or private, LLC or C-Corp."

One constant that will remain regardless of stage is RA Capital's desire to infuse enough money into companies so they can pursue multiple programs in parallel. The goal is to own biotechs that do not live or die based on one binary event.

UNCONVENTIONAL UPBRINGING

RA Capital is named after Richard Aldrich, a co-founder of [Vertex Pharmaceuticals Inc.](#), and began life in 2001 when he hired Kolchinsky to manage about \$4 million.

Kolchinsky's first job was triaging the portfolio. "We discovered the discipline of not looking backwards at cost basis, but asking the question 'if we didn't have the stock today, would we be buying it?'" he said. "If the answer was 'no,' we sold it."

The firm's early wins included an investment in HIV company [Triangle Pharmaceuticals Inc.](#), which [Gilead Sciences Inc.](#) acquired for \$464 million in cash in early 2003.

Rajeev Shah joined RA Capital in 2004 and he and Kolchinsky increased the pace of analyzing companies and set about challenging the conventional wisdoms about investing.

For example, Kolchinsky and Shah challenged the notion that the stock of companies short on cash suffered from a financing overhang. "If everybody is afraid of the overhang, there's going to be a buildup of demand and you might be better off buying the stock on the open market instead of waiting to buy it in an offering," said Shah. "The notion of an overhang didn't apply to good companies. That was evident in the data, but it was conventional wisdom that caused people to miss out."

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PETER KOLCHINSKY, RA CAPITAL

Shah added, "Sometimes we stepped up when no one else would, so we basically built a position and made the financing overhang go away at the same time."

PRIVATE LIFE

RA Capital made one of its first private investments in 2010 when it participated in a \$15 million series C round for diagnostic company [T2 Biosystems Inc.](#)

"T2 was compelling because our diligence on antibiotics kept telling us that physicians could do a lot more with the drugs they already had if only they could know sooner which bugs were making a patient sick, within hours instead of days. T2 had evidence they could crack this problem, so we wanted to be on the right side of what seemed like a likely disruptive innovation," said Kolchinsky.

T2 markets its T2Candida Panel to detect sepsis-causing *Candida*. For the next two years, T2 was one of only a few recipients of RA's private dollars.

Things changed in 2012 when RA began to explore the private markets in earnest. The private push coincided with two events, one internal and the other external.

Outside the firm, the markets were heating up and biotech was leading the pack. The reemergence of a biotech IPO window meant there was an arbitrage opportunity. Firms able to participate in a biotech's mezzanine round could be promptly rewarded with a step-up in valuation when the company went public.

Internally, RA had formed its TechAtlas research division, which now consists of about 40 employees dedicated to making detailed maps of a given therapeutic area.

The maps look at standard of care, and then delve into all industry pipeline programs for the disease, analyzing competitive strengths and weaknesses and the potential for combinations (see "TechAtlas Drugged").

From those maps, RA looks for companies with the best solution set for a disease or therapeutic area.

In some cases, the maps showed that a private company's asset trumped what was available among public companies.

For example, Kolchinsky said, RA's research on [Pain Therapeutics Inc.](#) led the firm to [Collegium Pharmaceutical Inc.](#) In 2015, RA participated in Collegium's \$50 million series D round. Both companies are developing abuse-deterrent compounds for pain.

The firm now is one of the most active crossover investors in biotech. Since the start of 2012, RA Capital has invested in private financings for at least 45 biotech companies. Of those, 23 are now public.

"We focus on making sure our companies are well capitalized," said Kolchinsky. "A great team, especially a well-resourced team, can do great science and come up with lots of options and the companies stop being so binary. The science being done today throughout the industry merits more capital."

Beginning in 2012, the median sizes of series A, B and C rounds in which RA Capital participated were \$23.3 million, \$46.5 million and \$52.5

TECHATLAS DRUGGED

RA Capital's TechAtlas research division analyzes and maps broad swaths of biology to help drive its investment decisions. Below is an excerpt from the firm's B cell malignancy map, which informed RA Capital's investment in [TG Therapeutics Inc.](#) (NASDAQ:TGT). Although no single TG asset is the most advanced in a given category, the firm views TG as the most solution-oriented, rather than asset-oriented, biotech focused on B cell malignancies. *Source: RA Capital*

	Must-Haves				Add-ons/Follow-ons		
	Anti-CD20 mAbs	B cell receptor pathway inhibitors		BCL-2 inhibitor	Oral EZH2 inhibitor	Checkpoint inhibitors/agonists	
		BTK	PI3K-δ				
Individual assets for assimilation		••• BeiGene • Principia • Sunesis	• Incyte • Rhizen	•• ProNAi (DNAi)	••• Epizyme • Constellation	•• Medivation (MOA unclear; formerly anti-PD1)	
TG Therapeutics	••• Ublituximab		••• TGR-1202			• Anti-PD-L1; anti-GITR (w/ Checkpoint/Fortress)	
Solution Developers	M Rituxan M Gazyva			NDA (for CLL) Venetoclax (w/ AbbVie)			
Roche							
JNJ		M Imbruvica (w/ AbbVie)					
Gilead		• GS-4059 (w/ Ono)	M Zydelig				
AbbVie		M Imbruvica (w/ JNJ)	••• Duvelisib (w/ Infinity)	NDA (for CLL) Venetoclax (w/ Roche)			
AstraZeneca		••• Acalabrutinib (w/ Acerta)	••• ACP-319 (w/ Acerta)			••• Anti-PD-L1 (w/ Celgene) ••• Anti-OX40	
Novartis	M Arzerra			• (w/ Servier)			
Bristol-Myers Squibb						•• Anti-PD1 • Anti-CTLA4	

million. By comparison, the overall industry averages in the same time frame were \$15.7 million for a series A, \$25.1 million for a series B and \$29.1 million for C rounds.

A key lesson was that longer timelines allowed the firm to better acquaint itself with executives compared with public biotechs.

“In the public domain, sometimes a breakthrough happens and you have to make a decision in a short time frame. You look at the data and then you look at the people and make a decision before you have really gotten to know them and how well they can execute,” said Kolchinsky. “It’s a different dynamic in the private markets — you have the time to get to know management teams.”

Another private company lesson was that “sometimes it’s good to be stuck in a stock because you get to see them overcome challenges,” said Kolchinsky. “Sometimes companies would drive a preclinical candidate forward and encounter an unexpected result. You don’t like getting such news but there’s nothing for the shareholders or directors to necessarily do but to stay the course. A few months later the company would fix the issue and show the problem was not drug-related. A public company might have had to issue a scary-sounding press release, and the stock probably would have plummeted as investors sold first and asked questions later. With patience, a good company can find a way to succeed — the lessons we have learned on the private side have made us better on the public side.”

The firm does not disclose its returns on private companies.

EARLIEST BIRD

Last year saw RA Capital invest in early rounds of several companies, including participation in series A financings for [Qvella Corp.](#) and [Taris Biomedical LLC](#).

Qvella is developing molecular diagnostics that detect pathogens via direct sampling of bodily fluids.

Taris is developing bladder disease therapeutics using LiRIS, a lidocaine-releasing intravesical system that provides continuous local delivery to the organ.

The firm also invested last year in the series A round of [Wave Life Sciences Ltd.](#), which was formed in 2012 from the merger of [Ontorii Inc.](#) and [Chiralgen Ltd.](#)

Wave is focused on stereopure nucleic acid therapeutics for indications including Huntington’s disease and Duchenne muscular dystrophy (DMD).

The next step, said Kolchinsky, is going upstream of series A and starting companies from scratch.

“I don’t view us as a crossover fund anymore,” he said. “We want to maximize optionality and ownership stake.”

“We’re talking to company builders,” he added. “To attract those people, we’re becoming an institution that gives innovators everything they need to execute on their ideas.”

In almost all cases, RA Capital expects the endgame will be acquisitions by big biotech and pharma.

“It’s plausible that one of these large giants will simply say, ‘I need growth more than you and I’m willing to pay the price,’” said Kolchinsky.

The firm’s most recent M&A exit was [Dyax Corp.](#), a developer of therapies for hereditary angioedema (HAE). This year, [Shire plc](#) completed the acquisition for \$37.50 per share, or \$5.9 billion in cash.

RA first invested in Dyax in 2011 when the stock was trading around \$1. In 2013, RA led a \$30 million financing for Dyax at a share price of \$2.30. [bc](#)

COMPANIES AND INSTITUTIONS MENTIONED

[Collegium Pharmaceutical Inc.](#) (NASDAQ:COLL), Canton, Mass.

[Gilead Sciences Inc.](#) (NASDAQ:GILD), Foster City, Calif.

[Pain Therapeutics Inc.](#) (NASDAQ:PTIE), Austin, Texas

[Qvella Corp.](#), Richmond Hill, Ontario

[RA Capital Management LLC](#), Boston, Mass.

[Shire plc](#) (LSE:SHP; NASDAQ:SHPG), Dublin, Ireland

[Taris Biomedical LLC](#), Lexington, Mass.

[T2 Biosystems Inc.](#) (NASDAQ:TTOO), Lexington, Mass.

[Vertex Pharmaceuticals Inc.](#) (NASDAQ:VRTX), Boston, Mass.

[Wave Life Sciences Ltd.](#) (NASDAQ:WVE), Cambridge, Mass.

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