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Ebb & Flow Focus

Clear route to Phase IIb

By Mike Ward
Senior Editor

Although big series A rounds have become increasingly commonplace, the recent deal for **Albireo AB**, expected to reach $40 million, reflects business as usual for **Nomura Phase4 Ventures.** The London firm has taken an aggressive approach to investing its parent's money in biotech, characterized by large financing rounds geared to providing a clear route to Phase IIb data, underpinned by international syndication.

Phase4's story is one of increasing scale, with rounds mounting in size from 1999 until the VC hit its stride in 2004. Since then, the firm has usually taken the lead in $1.3 billion worth of venture rounds.

"We were doing big rounds before it was really fashionable to do so," Managing Director Denise Pollard-Knight told BioCentury. "Since 2004, we haven't done any less than $15 million in a first-time investment, and most have been $20-$25 million."

In 1999, when Japanese bank **Nomura Group** created the VC to make biotech investments off the parent's the balance sheet, rounds were much more modest.

"Early on, we had to show that we could compete with the peer group and give the bank confidence that we would be able to return cash earlier," Pollard-Knight said. "We had to deliver exits to Nomura from both an IRR and a return on capital perspective."

Even then, the scale was larger. In 1999, Phase4 participated in five rounds where the syndicates averaged just under $20 million, at a time when the average deal for all VCs was just under $10 million. Nevertheless, only one of Phase4's transactions was among that year's 20 biggest venture financings.

In 2000, the average size of a round involving Phase4 had crept up to $29 million, and by 2001, it was topping $31 million. In that year, the average venture round globally was just under $15 million, and four of Phase4's 10 financings were among the industry's top 20 biotech venture deals.

"In the early days, we used to make initial investments of about $5-$10 million, as we were still proving ourselves at Nomura," said Pollard-Knight. "These days, in terms of our core strategy, we tend to put in $15-$20 million as an initial investment with the potential to follow on up to a total of $30-$40 million per company."

Indeed, the average size of the 10 most recent rounds Phase4 Ventures has participated in is a touch over $50 million. This is more than two and a half times the average biotech venture round over the same period.

Phase4 has participated in three series A rounds in the past three years in which the syndicates committed a total of $162 million to the three companies.

The firm focuses primarily on investment in clinical stage companies and as a result has a portfolio that is heavily biased toward the U.S. Over 75% of the companies Phase4 invests in are in Phase I or II, with an average holding time of about five years.

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>
> **— Phase4's Denise Pollard-Knight**

"We decided from the get-go to focus on clinical-stage product stories, which was contrarian at the time, as it was just ahead of the genomics bubble," Pollard-Knight said. She said the VC believed product assets were more tangible and easier to evaluate from a fundamental perspective.

One thing the deals have in common is that "they fit into a mold of not only having a lead program that we can see achieving clinical proof of concept reasonably quickly and so driving the initial valuation, but they also have other clinical or preclinical compounds and the capacity to generate a pipeline," Pollard-Knight said.

"You need to bring enough cash to get to the key value inflection points," she added. "No matter how early you start, you have to be able to see your way to that milestone."

As a consequence, most of the firm's portfolio companies are in or have completed Phase II/IIb, and several of its companies are now in Phase III.

More importantly, the VC has made money for Nomura Group, its sole backer. Since 1999, Phase4 has participated in 39 venture financings for 29 companies, exited nine of the companies it has backed, including six through M&A, and partially exited four more *(see "Nomura's Investments")*.

In 2004, the bank established Phase4 Ventures as a subsidiary. At that point, Nomura grouped the 1999-2004 portfolio into a fund-like structure, "so now we essentially have two

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funds," said Pollard-Knight. "From outside, these two funds look like a single evergreen fund, even though we have different buckets internally and have been able, where appropriate, to do crossover investments from the second fund into companies in the first fund."

The firm continues to build a portfolio covering the spectrum from classical drug discovery/development biotechs, through specialty pharma companies to pharma spinouts.

Early lessons

Phase4's approach has evolved as the result of lessons learned from the early deals. One was the 1999 investment in **Idenix Pharmaceuticals Inc.**, which was then an antivirals play called Novirio Pharmaceuticals Inc.

The firm participated in a relatively modest $12.5 million B round based on the company's NV-01, a nucleoside analog reverse transcriptase inhibitor that had potential against HIV. The company also had antiviral discovery capabilities.

Initially, Phase4 had not anticipated that Idenix would require much money to get to Phase II data. "The money was supposed to get NV-01 to the end of Phase II proof of concept, but we had to stop the program just over six months after we invested due to problems with PK," said Pollard-Knight.

Idenix's management, led by CEO Jean-Pierre Sommadossi, killed off the NV-01 program and used the cash to move forward a nucleoside analog, which later became Tyzeka telbivudine (Sebivo in EU), that had shown some preclinical promise in HBV, as well as NM 283, a nucleoside analog for HCV. Sebivo was approved to treat HBV in late 2006.

"By dropping the HIV program very early and refocusing the money they already had, we were able to get good proof-of-concept data in HBV," Pollard-Knight said. "After that the company went out and raised a much bigger round. It was a transformed company."

According to Pollard-Knight, Phase4 learned a number of lessons from the Idenix deal, including the need to kill failing compounds early and have a back-up that is IND-ready. For the company to do that, it would need more money.

Nomura participated in the $44 million series C round in 2001, bringing the total amount of money Idenix had raised to $70 million.

Idenix tried and failed to raise up to $115 million in an IPO in 2002.

In March 2003, when the IPO window was closed and M&A seemed unlikely, Idenix sold a 51% stake to Novartis for $255 million in cash plus up to $357 million in milestones. That deal, which emerged from licensing discussions, put a $500 million to $1.2 billion value on the biotech, depending on the milestone payments.

Idenix then raised $64.4 million in an IPO in July 2004 through the sale of 4.6 million shares at $14 that valued the company at $668.9 million.

Nomura still holds a small position in Idenix.

Banking on management

In the case of Idenix, it was management's ability to execute a course correction that saved the company. Another of the VC's best investments was based from the start on the potential of the management team to execute the business plan, coupled with the promise associated with its two lead programs.

Phase4 led a $65 million series B round in **Pharmion Corp.** in 2001. At that time, the company's lead compound, Vidaza azacitidine, had already been in-licensed from the Pharmacia Corp. unit of **Pfizer Inc.** The candidate had been through Phase III trials in myelodysplastic syndromes (MDS), although the data needed to be pulled together.

Pharmion also was finalizing a deal to in-license European rights to **Celgene Corp.**'s Thalomid thalidomide for refractory multiple myeloma (MM) and erythema nodosum leprosum (ENL).

"The key products that they'd in-licensed had lots of potential. We were backing the management on executing the regulatory strategy and building a commercial infrastructure. The CEO, Pat Mahaffy, had been at NeXstar and had demonstrated a capability of building a commercial team," said Pollard-Knight. "We saw it as a very late-stage product play."

NexStar Pharmaceuticals Inc., which was an anti-infectious disease company with two marketed products and a pipeline, had been acquired by **Gilead Sciences Inc.** for $550 million in stock.

Phase4 participated again in the 2002 $40 million series C round. In total, Pharmion raised $129 million in three venture rounds.

With Pharmion, Phase4 got an IPO within three years after the initial investment.

The company priced its offering at $14 in November 2003, raising $84 million and valuing the company at $335 million. Even better, "within a month of the lockup coming off, the team got Vidaza through the FDA."

FDA approved Vidaza to treat MDS in May 2004. The shares rose by $10.96 (40%) to $38.56 in the week after the approval.

Phase4 has exited the stock. In March, Pharmion was acquired by Celgene for $2.9 billion.

Safer havens

As with its investment in Pharmion, Phase4 was attracted to **Cerimon Pharmaceuticals Inc.** and **Phenomix Corp.**

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because they were clinical stage companies with portfolios considered to be fairly low risk.

Phase4 participated in Cerimon's $70 million series A in 2005 because the company was looking at fairly well characterized molecules with reduced regulatory risk but high market potential.

"When we were investing, they already had the topical patch formulation of diclofenac sodium in the clinic for pain indications and were finishing deal negotiations with Novartis over the use of the Simulect monoclonal in ulcerative colitis," Pollard-Knight said. "We saw the diclofenac patch as essentially underwriting our investment, but we also had the potential of using an approved monoclonal product in a different indication."

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> **— Phase4's Denise Pollard-Knight**

In February 2006, Cerimon licensed exclusive worldwide rights to Novartis' Simulect basiliximab to treat inflammatory bowel disease (IBD), including ulcerative colitis.

The chimeric mAb against interleukin-2 (IL-2) receptor on activated T cells is in a Phase IIb study in UC. Novartis markets the product for transplantation indications.

The diclofenac patch is in two Phase II/III trials to treat pain due to acute mild to moderate ankle sprains and pain due to mild to moderate tendonitis or bursitis.

Pollard-Knight highlighted Phenomix as characteristic of the drug development deals the Phase4 team would like to continue to do. She noted the company has a "fast follower approach based on medicinal chemistry expertise applied to clinically validated targets."

By aiming for best-in-class compounds, including ones with superior safety profiles, Phase4 believes Phenomix is reducing its risk and the time required to advance a product candidate into clinical trials. Indeed, the biotech says it advanced PHX1149 into the clinic 27 months after starting its dipeptidyl peptidase-4 (DPP-4) inhibitor discovery program.

PHX1149 is in a Phase IIb trial for Type II diabetes, with Phase III testing expected to begin in 2H08. Phenomix's second candidate is PHX1766, an HCV protease inhibitor in preclinical studies.

Phase4 led a $55 million series C round in March 2007 when the company had just got Phase IIa data for PHX1149. In January, Phenomix filed for an IPO.

Spinouts

In its desire to fund businesses with a clear route to clinical proof of concept, it is hardly surprising that Phase4 has emerged as an active participant in the spinning out of non-core assets from pharma and biotech companies. It sees these deals as another risk-reduction strategy that is built around established data packages.

In the last two years, Phase4 has led large funding rounds for three pharma spinouts, the most recent being gastrointestinal disease company Albireo from **AstraZeneca plc** in February.

Previously, Nomura led rounds for **Nabriva Therapeutics Forschungs GmbH**, which spun out of Novartis's **Sandoz AG** unit in January 2006, and the October 2006 spinout of Macroflux Corp., now **Zosano Pharma Inc.**, from **Johnson & Johnson**'s **Alza Corp.** subsidiary.

Its first spinout, **Altus Pharmaceuticals Inc.**, came from **Vertex Pharmaceuticals Inc.** in 2001.

Pollard-Knight likes building companies around IP spun out of pharma because the assets tend to be well characterized. "You get pharma packages around the compounds you are taking out. So long as the deal is reasonable from a valuation and retained rights perspective, you can generate Phase II data with an average-size financing," she said.

For example, Pollard-Knight noted, "although Nabriva was only about to go into Phase I with the lead program, they had a lot of compounds in the company that were well characterized from a preclinical package perspective. With a reasonable amount of capital, we could see a way of getting two compounds to Phase II clinical endpoints."

Sandoz spun out its Antibiotic Research Institute into Nabriva to develop antibiotics for community- and hospital-acquired infections. The newco had four preclinical compounds, one of which was slated to enter Phase I trials for respiratory infections within 12 months.

Phase4 led the $51 million series A round. Other investors included HBM Partners, the Wellcome Trust, Global Life Science Ventures and Novartis Venture Fund.

Pollard-Knight sees that deal as similar to the one for Albireo, which acquired an undisclosed compound from AstraZeneca that has completed Phase I testing and is in development for severe chronic constipation in geriatric patients and for drug-induced constipation. Albireo also has an undisclosed number of preclinical GI programs, including ones for functional dyspepsia, irritable bowel syndrome (IBS) and IBD.

The series A round, which is expected to total $40 million, is designed to provide Phase IIb data for the lead program and to fund an additional Phase II program for an as yet unidentified compound. At the first close, Albireo had raised $27 million and was waiting on an additional investor to sign off.

Similarly, when Phase4 led the October 2006 spinout of Zosano, Pollard-Knight could see a clear route to the end of Phase IIb for the company's parathyroid hormone (hPTH 1-34) transdermal microprojection delivery system to treat post-menopausal osteoporosis. The company completed enrollment of the Phase II trial ahead of schedule in November 2007.

While spinouts usually provide fairly robust data packages, they don't always come with fully fledged management teams. In each case, Nomura has parachuted in experienced executives who have helped pull the plan together.

At Zosano, Judith Hemburger, who had worked with Phase4 as a venture partner since her days as EVP and COO at Pharmion, was instrumental in working with J&J, Nomura and the syndicate including NEA to create an investable thesis around the assets.

Similarly, David Chiswell, founder and former CEO of Cambridge Antibody Technology plc, was installed at both Nabriva

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and Albireo to manage the spinout process before the financings were closed. Chiswell is chairman of Nabriva and executive chairman at Albireo.

Conceptual focus

The Phase4 team is not just cherry-picking companies with established technologies and lower regulatory risk profiles. It is also prepared to take on challenging science, but again, only if it can see a clear route to clinical proof of concept, defined as the opportunity to achieve at least two Phase II clinical endpoints with one or two compounds.

Phase4 led the $53 million 2006 series C financing in U.K. oncology and inflammation play **Chroma Therapeutics Ltd.** when it had only limited Phase I data for its lead program, CHR-2797.

"What was impressive was the breadth of the company's biology, medicinal chemistry and drug discovery experience," said Pollard-Knight.

Chroma targets inhibition of chromatin-modifying enzymes using a quasi-prodrug approach that allows specific targeting of macrophages and uses intracellular enzymes to split the carrier from the active inhibitor.

The investors anticipated that the company would use the funds to develop CHR-2797 through Phase II and to move its HDAC and aurora kinase inhibitors into the clinic.

At the time of the financing, CHR-2797, an aminopeptidase inhibitor, had entered Phase I after demonstrating anti-tumor activity in preclinical models both as monotherapy and in combination with cytotoxic agents.

CHR-2797 subsequently has shown signs of efficacy in Phase I studies in both hematological and solid tumors. It is in a Phase II study in treatment-refractory acute myeloid leukemia (AML) as monotherapy and recently started a Phase II combination study in non-small cell lung cancer (NSCLC).

This year, Chroma is expected to start clinical development of an oral HDAC inhibitor, CHR-3996.

More chemistry & biology

Similarly, when Phase4 went looking for an entry into the CNS space in 2001, it specifically looked for companies that could marry chemistry and biology to drive development of compounds focused on well-established therapeutic targets.

As a result of that review, Phase4 led the 2002 $60 million series B investment in **Targacept Inc.**, in 2005 led a PIPE for **Acadia Pharmaceuticals Inc.**, and put money into **ARYx Therapeutics Inc.** in 2004.

"At the time we invested in Targacept, the company had done a great job of establishing a broad portfolio of clinical-stage CNS opportunities based on a combination of nicotinic acetylcholine receptor biology and medchem to identify selective drug candidates with promising safety profiles," said Pollard-Knight. "They had some Phase I data at the time and had a number of compounds ready to go into Phase II."

Targacept had developed a method for identifying compounds that could selectively target disease-specific neuronal nicotinic receptors (NNRs), with the goal of achieving therapeutic effects while limiting or eliminating the side effects associated with off-target NNRs.

At the time, Targacept was focusing on Alzheimer's disease (AD), Parkinson's disease (PD), dementia with Lewy bodies (DLB), ulcerative colitis, depression, pain, anxiety disorders and schizophrenia. It had an AD alliance with Aventis Pharma S.A., now **sanofi-aventis Group**, and an alliance with **Dr. Falk Pharma GmbH** to develop UC treatments. Both alliances have since been dissolved.

Since 2002, Targacept has completed a $45 million IPO and an additional public offering of $30.9 million, as well as signing two alliances with AstraZeneca and **GlaxoSmith-Kline plc**.

AstraZeneca is Targacept's partner for lead program AZD3480 (TC-1734), a small molecule nicotinic acetylcholine alpha(4)beta(2) receptor agonist in Phase IIb testing in mild to moderate AD and for cognitive deficits in schizophrenia.

AstraZeneca also has an option to license TC-5619, a small molecule that modulates the neuronal nicotinic receptor subtype alpha 7. It is in Phase I for schizophrenia and cognitive impairment.

The GlaxoSmithKline deal gives the pharma access to programs in five therapeutic areas: pain, smoking cessation, obesity, addiction and PD. The lead program is TC-6499, a modulator of the nicotinic acetylcholine receptor alpha(4)beta(2) in Phase I for neuropathic pain.

Targacept is developing a similar molecule, TC-2216, under its own steam. TC-2216, which is also a nicotinic acetylcholine receptor alpha(4)beta(2) modulator, is being developed as an oral monotherapy for depression and anxiety disorders. It is in Phase I.

With Acadia, Phase4 began following the company in 2002, when it was still private, before finally investing in a PIPE in 2005.

"We liked the fact that the company had taken compounds from a classical screening/medchem approach against validated receptor targets into the clinic, with multiple shots on goal and a clearly experienced development team," noted Pollard-Knight.

In 2002, Acadia's lead program, pimavanserin tartrate (ACP-103), a small molecule serotonin (5-HT2A) receptor inverse agonist, was about to go into the clinic. All other programs were still in early preclinical development. Consequently, the company was considered still a little too early for Phase4.

By the time Phase4 corner-stoned the $36 million PIPE, Acadia had started Phase II trials of ACP-103 for PD and as an adjunct for schizophrenia. ACP-104, a metabolite of clozabine and partial agonist of dopamine D2 and D3 receptors, was in Phase I for schizophrenia.

Pimavanserin now is in an international Phase III trial to treat PD and has completed a Phase IIb trial to treat schizophrenia, while ACP-104 is in a Phase IIb trial in patients experiencing an acute psychotic episode.

As with Acadia, Phase4 waited until ARYx's programs had matured with convincing clinical data before its $55 million series D investment in 2004.

"We tracked the company for some time from preclinical to early clinical and then when they were ready and needed a larger financing we already knew the company, management and investors," said Pollard-Knight.

Phase4 liked ARYx's retrometabolic chemistry approach,

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which is designed to engineer out safety problems, such as cytochrome P450 metabolism and QTc prolongation, in existing compounds.

Based on this approach, ARYx had moved two products into the clinic. "When we invested in ARYx, they had Phase I data on their lead program, ATI-7505, and had ATI-2042 in a Phase I study," Pollard-Knight noted.

ATI-7505, an oral serotonin (5-HT4) receptor agonist that is structurally similar to J&J's Propulsid cisapride, is in development to treat gastroesophageal reflux disease (GERD) and gastroparesis. Since Phase4 first invested, the compound has been partnered with **Procter & Gamble Co.** and has completed or is in a number of ongoing Phase II trials in various GI disorders.

ATI-2042 is an oral anti-arrhythmic designed to have a similar therapeutic effect but be more easily metabolized than amiodarone, a drug that has been used for many years despite its adverse side effects.

Since Nomura's initial investment, ARYx has finished one pilot Phase II trial in patients who suffer from repeated episodes of atrial fibrillation or paroxysmal atrial fibrillation, and is running a larger Phase II trial in the latter condition.

ARYx, which raised an additional $30.4 million in a series E round in February 2006 and completed a $50 million IPO in November last year, is also moving forward with ATI-5923, a selective vitamin K epoxide reductase (VKOR) inhibitor as a potential treatment for atrial fibrillation, valvular heart disease and deep vein thrombosis (DVT). It is in a Phase II trial to assess its safety and efficacy over warfarin, an anti-coagulant that is sometimes prescribed to treat atrial fibrillation.

ARYx's lead CNS candidate, ATI-9242, which Nomura first flagged in its sectoral review, is due to enter the clinic as a potential schizophrenia treatment this year. The compound is an atypical antipsychotic designed to eliminate the serious side effects that plague most compounds in this area, such as reduction of white blood cells, or agranulocytosis.

Phase4 still holds positions in Targacept, Acadia and ARYx.

Vaccine exposure

As the vaccines space became increasingly interesting at the end of the 1990s, Phase4 decided to review opportunities in that arena. The firm opted to invest in one of the less developed players in the space, **Intercell AG**, because the VC believed in the company's platform.

Nomura participated in a €27 million ($25.9 million) series B round in January 2001, which also involved TVM and Global Life Science Partners. At the time, Intercell had nothing in the clinic. "This was a large financing at the time and was focused on getting something into the clinic prior to a next funding round," said Pollard-Knight.

"While other companies we looked at had vaccine candidates in the clinic, it was clear to us that Intercell's antigen and adjuvant discovery capabilities would be the foundation of a potentially sustainable vaccines business," she noted. Moreover, the team believed that the management would be able to marry the biology with the chemistry, a strong theme running through much of Nomura's investment strategy.

Since 2001, the company has established several pharma partnerships, including Novartis, **Merck & Co. Inc.**, **Wyeth** and sanofi-aventis' **sanofi pasteur vaccines** unit. Its lead program, a prophylactic vaccine against Japanese encephalitis which is in registration in both the U.S. and Europe, was in-licensed in 2003 from **VaccGen International LLC** at the behest of the company's management. The vaccine had completed a Phase II U.S. trial.

"In 2003 it was not common for biotechs to in-license," Pollard-Knight noted. "We are glad we listened, as that move has created a lot of value for the company."

The company also has a Pseudomonas vaccine in Phase II, a therapeutic vaccine for HCV in Phase II, partnered vaccines for *Staphylococcus aureus* in Phase II and for tuberculosis in Phase I, and five vaccine candidates focused on infectious diseases in preclinical development.

With Intercell being based in Austria, part of Nomura's plan was to help build international investor support for the company. In March 2005, Intercell raised €46.8 million ($61.9 million) through the sale of 8.5 million shares at €5.50 on the Viennese stock exchange, not well known for attracting international investors. At the IPO, Intercell had a valuation of €181.6 million ($240.5 million).

For Pollard-Knight, it is important to bring in international partners who share a vision of where a company is going and what an exit plan might be.

"In Europe, we find it very useful to have U.S. investors in the syndicates because it does introduce different thinking to the table," she said.

There is also the opportunity to tap into other sources of deep capital to drive development.

Phase4 no longer holds shares in the company.

— Senior Writer Stacy Lawrence contributed to this report

COMPANIES AND INSTITUTIONS MENTIONED

Acadia Pharmaceuticals Inc. (NASDAQ:ACAD), San Diego, Calif.
Albireo AB, Gothenburg, Sweden
Altus Pharmaceuticals Inc. (NASDAQ:ALTU), Cambridge, Mass.
ARYx Therapeutics Inc. (NASDAQ:ARYX), Fremont, Calif.
AstraZeneca plc (LSE:AZN; NYSE:AZN), London, U.K.
Celgene Corp. (NASDAQ:CELG), Summit, N.J.
Cerimon Pharmaceuticals Inc., South San Francisco, Calif.
Dr. Falk Pharma GmbH, Freiburg, Germany
Gilead Sciences Inc. (NASDAQ:GILD), Foster City, Calif.
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Idenix Pharmaceuticals Inc. (NASDAQ:IDIX), Cambridge, Mass.
Intercell AG (VSE:ICLL), Vienna, Austria
Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.
Merck & Co. Inc. (NYSE:MRK), Whitehouse Station, N.J.
Nabriva Therapeutics Forschungs GmbH, Vienna, Austria
Novartis AG (NYSE:NVS; SWX:NOVN), Basel, Switzerland
Pfizer Inc. (NYSE:PFE), New York, N.Y.
Pharmion Corp. (NASDAQ:PHRM), Boulder, Colo.
Phenomix Corp., San Diego, Calif.
Procter & Gamble Co. (NYSE:PG), Cincinnati, Ohio
sanofi-aventis Group (Euronext:SAN; NYSE:SNY), Paris, France
Targacept Inc. (NASDAQ:TRGT), Winston-Salem, N.C.
VaccGen International LLC, Larchmont, N.Y.
Vertex Pharmaceuticals Inc. (NASDAQ:VRTX), Cambridge, Mass.
Wyeth (NYSE:WYE), Madison, N.J.
Zosano Pharma Inc., Fremont, Calif.

Nomura's investments

Nomura Phase4 Ventures has invested in at least 25 biotechs since 1999. Usually Nomura's contribution for an initial investment will be some $15-$25 million of the round, although in subsequent rounds it can go up to a total of $30-$40 million per company. Prior to 2004, Phase4's share in a round was unlikely to exceed $15 million, whereas post-2004, it is more likely to be on the order of $25 million. Over the years, Nomura has completely exited nine of its investments, including six from M&A and three from IPOs, and partially exited four undisclosed investments. The list below does not include medical device companies. (A) Completely exited; *Source: Nomura Phase4 Ventures; BioCentury Online Intelligence — BCIQ*

Company	Description	Year of initial investment	Total raised in financings involving Nomura	Additional investors
Avant (NASDAQ:AVAN), merged with **Celldex** (A)	Developing vaccines leveraging bacterial vector delivery technologies	1999	$11M PIPE, 1999	Institutional investors
DrugAbuse Sciences, certain assets acquired by **elbion** in 2007	Developed therapeutics to treat and prevent drug addictions	1999	$22M series D, 1999	3i; ABN AMRO; Auriga Ventures; CDC Ixis Innovation; Edmond de Rothschild Investment Partners; Financiere de Brienne; Parnib Belgie; Partech International; SG Asset Management
			$24M series E, 2001	3i; Canaan Partners
			$6M bridge, 2005	3i; CDC Capital Partners; CDC Entreprises Innovation; Canaan Partners; Philippe Pouletty
Idenix (NASDAQ:IDIX)	Biopharmaceutical focusing on creating drugs for infectious diseases	1999	$13M series B, 1999	MPM Capital; TVM Capital
			$44M series C, 2001	Banc of America Securities; Biomedical Sciences Investment Fund; Credit Suisse First Boston Private Equity; Hanseatic Corp.; MPM Capital; Novartis BioVenture Fund; Swan Private Equity; Swiss Life Private Equity Partners; TVM Capital
Sequenom (NASDAQ:SQNM) (A)	Genetic analysis company	1999	$37M series D, 1999	Alafi Capital; AlpInvest; Deutsche Bank; Dresdner Kleinwort; Euroventures; Haspa Bank; Global Life Sciences; S.R. One; Value Management & Research; TVM Capital; Vertex Venture Capital Isarel
Weston Medical, acquired by **Aradigm** (OTCBB:ARDM) (A)	Developed needle-free drug delivery	1999	$13M venture, 1999	3i; Phildrew Ventures
Ark (LSE:AKT) (A)	Specialist healthcare company focused on vascular disease and cancer	2000	$23M series A, 2000 (as Eurogene)	Merlin Biosciences; Mountcashel, TVM Capital; BioFund; Concordia; Sampo Insurance
			$21M series B, 2001	BankInvest; BioFund; Merlin Biosciences; TVM Capital
Immgenics, acquired by **Abgenix** which is now part of **Amgen** (NASDAQ:AMGN) (A)	Developed rapid antibody screening technology	2000	$10M series B 2000	International Biotechnology Trust

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Company	Description	Year of initial investment	Total raised in financings involving Nomura	Additional investors
Morphochem, acquired by **Biovertis** (A)	Focused on developing anti-microbials	2000	$38M series C, 2000	3i; Alta Berkeley Associates; Alta Partners; Domain Associates; IKB; Julius Baer; Merlin Biosciences; Techno-Venture; Viscardi GmbH; WestLB
			$13M bridge, 2001	Alta Berkeley Associates; Alta Partners; Life Science Venture Fund; Merlin Biosciences; TVM Capital; Viscardi GmbH; WestLB
Paratek	Focusing on therapeutics that combat antibiotic resistance	2000	$20M series C, 2000	BankInvest; BioFund; FSC Corp.; Lombard Odier
			$30M series D, 2002	BankInvest; BioFund; BioVeda; China Development Industrial Bank; GeneChem Therapeutic Venture Fund; HBM BioVentures; Lombard Odier; Novartis; POD Holding; Wheatley Partners
			$40M series H, 2007	Aisling Capital; BioFund; Boston Life Science Corp.; BioVeda; D.E. Shaw Group; HBM BioVentures; Hercules Technology Growth Capital; Lombard Odier; Novartis BioVenture Fund
Viacell, acquired by **Perkin-Elmer** (NYSE:PKI) in 2007 (A)	Focusing on women's health and is investigating therapeutic applications for umbilical cord blood-derived stem cells	2000	$49M series H, 2000	DWS Investment GmbH; Stephens; Economic Development Board of Singapore; Sofinov; United Offshore Bank
			$15M series I, 2001	Economic Development Board of Singapore; Genzyme Corp.; Stephens; Tullis-Dickerson & Co. Inc.; United Offshore Bank; Zero Stage Capital
Altus (NASDAQ:ALTU)	Developing oral and injectable protein therapeutics for GI and metabolic disease. The company was spun out of Vertex.	2001	$50M series B, 2001	BankInvest; CMEA Ventures; Clariden Bank; China Development Industrial Bank; Hotung Ventures; Palladian Group; U.S. Venture Partners
			$51M series C, 2004	BankInvest; CMEA Ventures; Clariden Bank; U.S. Venture Partners;Warburg Pincus LLC
Intercell (VSE:ICLL) (A)	Using technology platform to develop and manufacture vaccines and adjuvants	2001	$26M series B, 2001	GO Equity GmbH; Sal. Oppenheim; AlpInvest; Apax Partners; TVM Capital
			$50M series C, 2003	Apax Partners; Global Life Science Ventures; MPM Capital; NIB; Star Ventures; TVM Capital

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Company	Description	Year of initial investment	Total raised in financings involving Nomura	Additional investors
Pharmion (NASDAQ:PHRM), acquired by **Celgene** (NASDAQ:CELG) (A)	Focusing on development and commercialization of therapeutics for hematology and oncology	2001	$65M series B, 2001	Aberdare Ventures; Abingworth Management; Bay City Capital; Domain Associates; HealthCap; Invemed Associates; Merlin BioMed Group; Montagu Newhall Assoc.; New Enterprise Associates; NeoMed; ProQuest Investments; Versant Ventures; and company management
			$40M series C, 2002	Bay City Capital; General Electric; New Enterprise Associates; ProQuest Investments; Versant Ventures; and company management
Arakis, now a subsidiary of **Sosei** (Tokyo:4565)	Programs include chronic obstructive pulmonary disease (COPD) and cancer breakthrough pain	2002	$25M series B, 2002	3i; MB Venture Capital Fund; Merlin Biosciences
			$52M series C, 2004	3i Group; Close Finsbury Eurotech; MB Venture Capital Fund; Merlin Biosciences; Finsbury Life Sciences; Novo A/S; Scottish Equity Partners; Scottish Widows Investment Partnership; and company management and directors
Targacept (NASDAQ:TRGT)	Developing CNS therapeutics targeting neuronal nicotinic receptors	2003	$60M series B, 2003	Academy Ventures; Auriga Ventures; Bison Capital; Burrill & Co.; Advent Venture Partners; CDC Ixis Innovation; CDIB BioScience Venture Management; Cogene Biotech Ventures; Easton Hunt Capital Partners; Genavent Fund; JAFCO; New Enterprise Associates; Oxford Bioscience Partners; Rock Castle Ventures; SG Asset Management
			$33M series C, 2004	No additional investors
ARYx (NASDAQ:ARYX)	RetroMetabolic Drug Design technology expected to create safer oral therapies addressing various GI disorders	2004	$55M series D, 2004	ATEL Ventures; Itochu; JAFCO; MPM Capital; Merlin BioMed Group; Montreux Equity Partners; Novel Bioventures; OrbiMed Advisors; Scottish Widows Investment Partnership
			$30M series E, 2006	Ascent Biomedical Ventures; JAFCO; MPM Capital; Merlin BioMed Group; Montreux Equity Partners; Novel Bioventures; OrbiMed Advisors; Scottish Widows Investment Partnership
DeveloGen	Biopharmaceutical company targeting metabolic and endocrine disorders	2004	$23M series C, 2004	AlpInvest; Aventis; DVC Deutsche Venture Capital; Dansk Kapitalanlaeg; Global Life Science Ventures; TVM Capital

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Company	Description	Year of initial investment	Total raised in financings involving Nomura	Additional investors
Acadia (NASDAQ:ACAD)	Drug discovery platform to develop compounds for CNS	2005	$36M PIPE, 2005	Institutional Investors
Cerimon	Developing therapies for autoimmune diseases, inflammation and pain	2005	$70M series A, 2005	MPM Capital; OrbiMed Advisors
Atani	In-licensing Western drugs for development in Japan	2006	Not disclosed	NovaQuest
Chroma Therapeutics	Targeting chromatin-modifying enzymes (CMEs) to develop anti-cancer small molecules	2006	$52M series C, 2006	Abingworth Management; Essex Woodlands Health Ventures; Gilde; Wellcome Trust
Nabriva	Antibiotic company spun out of Sandoz in 2006	2006	$51M series A, 2006	Global Life Science Ventures; HBM Partners; Novartis Venture Fund; Wellcome Trust
Zosano	Developing transdermal drug delivery technologies. Spun out of Johnson & Johnson (NYSE:JNJ) in 2006.	2006	$90M series B, 2006	HBM Partners; New Enterprise Associates; ProQuest Investments
Phenomix	Developing small molecules for metabolic and infectious diseases. Filed for an IPO in late January.	2007	$55M series C, 2007	Alta Partners; Baker Brothers; Bay City Capital; CMEA Ventures; Delphi Ventures; GBS Venture Partners; JPMorgan Partners; Novartis BioVenture Fund; Sofinnova Ventures
Albireo	Focusing on developing functional GI compounds. The company was spun out of **AstraZeneca** (LSE:AZN; NYSE:AZN) this year.	2008	$27M series A, 2008	Scottish Widows Investment Partnership; TVM Capital