

Europe's New Spec Pharma Models

(A#2007800136)

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Issue: *IN VIVO* Sep. 2007

Section: Feature Articles (Long Article)

Article Type: Corporate Strategy; Corporate Strategy/M&A (Mergers, Acquisitions); Corporate Strategy/Marketing & Sales

Subject/Market Dynamic: Big Vs. Small Company; Business Development Strategies; Business Models; Company Valuations; Corporate Strategies; Dealmaking Strategies; Distribution Strategies; Exit Strategies; Financing Strategies; Geographic Carve-Outs; In-licensing-based companies; Internationalization Strategies; Local Markets; Marketing and Sales Strategies; Mid-Sized European Pharmaceutical Companies; Near-Term Biotech Strategies; Niche strategy; Primary Care Vs. Specialist; Product-Line Breadth; Regulatory strategies; Sales Strategies; Specialty Pharmaceuticals; Venture Capital Financing Strategies; Venture Capital Investment Areas

Geography: Asia/China; Asia/Pacific Rim/Japan; Europe; Europe/Western Europe; Europe/Western Europe/UK; North America; North America/USA

Companies: Archimedes Pharma Ltd.; Cephalon Inc.; Elan Corp. PLC; Endo Pharmaceuticals Holdings Inc./Endo Pharmaceuticals Inc.; Nitec Pharma AG; Pharmion Corp.; PowderMed Ltd./Circassia Ltd.; ProStrakan Group Ltd.; Rhei Pharmaceuticals Inc.; Shire Pharmaceuticals Group PLC; Zeneus Pharma Ltd.

Summary: Spec pharma has created significant value in the US, but not, so far, in Europe. Still, Europe's spec pharma hopefuls aren't giving up, and they're trying out variations on the theme—some starting with infrastructure, others with products.

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Europe's New Spec Pharma Models

Spec pharma has created significant value in the US, but not, so far, in Europe. Still, Europe's spec pharma hopefuls aren't giving up, and they're trying out variations on the theme—some starting with infrastructure, others with products.

Melanie Senior

The US spec pharma sector was built on an acquire-and-market model, at a time when undervalued or tail-end products were relatively abundant.

The same held for Europe, where fragmented markets made commercialization harder, but also made infrastructure more valuable.

Conditions have changed. Products are rarer and pricier, hence many new spec pharma, on both sides of the Atlantic, are focused on building a late-stage pipeline, with marketing just an ambition.

Others in Europe are staying closer to the older model, though, betting that regulatory and reimbursement hurdles will force drug developers to license out to those with the appropriate infrastructure and expertise.

When US-based **Cephalon Inc.** acquired Europe's **Zeneus Pharma Ltd.** in December 2005 for \$360 million, Zeneus' backers Apax Partners made three times their money, in a 22 month investment. [W#200510204] For a handful of European entrepreneurs and investors, the deal was an inspiration.

Zeneus was a pan-European in-licensing and marketing organization created from infrastructure discarded by then-troubled **Elan Corp. PLC**. Cephalon, having grown to well over \$1.5 billion in sales largely through shrewd in-licensing and commercialization skills, could no longer rely on the US for growth. There are others in the multibillion-dollar US specialty pharma sector that either are, or may soon be, in a similar situation. (*See Exhibit 1.*) Those looking to crack the complex and fragmented European market would probably prefer, like Cephalon, to buy a ready-made pan-national infrastructure than try to build their own.

Exhibit 1

Selected US Spec Pharma Winners

(including those that have since shifted upstream)

COMPANY NAME	MARKET CAP (\$bn, as of 8/21/07)
Gilead	35.2
Celgene	22.6
Shire Pharmaceuticals*	13.5
Cephalon	4.6
Endo Pharmaceuticals	4.2
King Pharmaceuticals	3.7
Sepracor	2.8
MGI Pharma	1.84
Pharmion	1.4

*officially UK-headquartered but majority US sales

SOURCE: FT.com; Yahoo Finance

That's why many of Europe's youngest generation of specialty pharma firms say their goal is to create another Zeneus. For others the *raison d'être* isn't simply to feed anticipated demand from bigger US counterparts—although this remains a highly comforting backdrop for investors. Some, like newly founded **EUSA Pharma Inc.**, have transatlantic ambitions of their own. Their model is **Shire PLC**, one of the most successful pioneers of the in-licensing and marketing-focused specialty pharma model.

Neither Zeneus nor Shire will be easy to copy, though. Zeneus inherited a ready-made pan-European infrastructure, and also had the right kind of products to attract Cephalon. Shire struck gold with the ADHD treatment *Adderall*, a mix of amphetamine salts—found via US acquisitions. Europe's aspiring spec pharma today face a double-layered challenge. They must build a focused product portfolio and infrastructure in a region defined by national differences while satisfying investors' demands for growth and revenues—the whole point of spec pharma. And they must do so at a time when the underlying conditions supporting the traditional spec pharma premise have worsened everywhere: there are fewer undervalued late-stage or marketed assets and more, and richer, hunters; meanwhile pricing and reimbursement pressure, especially in Europe, is pushing up the innovation hurdle.

These factors help explain why Europe has thus far failed to build a spec pharma sector that is anywhere near the value as that in the US, and why many public investors are less than impressed by the performance of some of those who've tried.

Nevertheless, the private equity and venture capitalists backing the latest generation of spec pharma are

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reassured by the fact that many are run by executives with experience within earlier successes like Shire or Zeneus. These people know how to spot and monetize undervalued assets, they argue. And in any case, product supply should be plentiful, as US biotechs seek Europe-focused commercial partners and as an increasingly complex regulatory environment puts some start-ups, both European and American, off commercialization altogether. In sum: the model is alive and well.

Specialty pharma isn't a single model, though. The label used to refer to firms that in-licensed and commercialized underexploited drugs to specialist prescribers. They took little or no R&D risk. If they did any drug development, it was the very tail end of the process. But these days, any drug development start-ups beginning life with late-stage, low-risk pipelines and commercial ambitions—including spinouts, re-profilers, and yesterday's drug delivery firms—are labelled specialty pharma. Some maintain R&D capabilities. Meanwhile, European biotechs have for years been forced by risk-averse investors to become quasi-spec pharma, too, buying in-marketed drugs to fund discovery. (*See "European Biotech Is Specialty Pharma," IN VIVO, May 2005 [A#2005800093].*)

The upshot: everyone's competing for specialist products. Infrastructure may still have more value in Europe than in the homogenous US market—there are relatively few pan-European specialist marketers. But in a product-poor environment, drug candidates are trumps. Thus one key battle for Europe's market-focused spec pharma—in their quest both for products, and, where appropriate, for acquirers—may play out within their own widening ranks: between those starting with a pipeline of late-stage drugs and a plan to market them, and those starting with an infrastructure and intending to attract others' assets to it. (*See Exhibit 2.*)

Exhibit 2

European Spec Pharma: Selected Newcomers

Infrastructure-Focused

COMPANY NAME	STRATEGIC AMBITION	ACQUISITIONS TO DATE
Specialty European Pharma	Pan-European S&M infrastructure, quick exit/sale	Proreo Pharma AG (Switzerland, product)
Archimedes Pharma	Pan-European S&M infrastructure focused on pain	West Pharmaceuticals (drug delivery); Link Pharmaceuticals (UK, infrastructure)
EUSA Pharma	Transatlantic S&M infrastructure in critical care, oncology, pain	Talisker Pharma (UK, product rights); OPi (France, products and some direct sales); Innocoll (Ireland, products and pan-Euro infrastructure)
ProStrakan	Transatlantic S&M infrastructure in urology/endocrinology, oncology supportive care	ProSkelia (bone R&D); OTL Pharma (France, infrastructure); Elfar (Spain, infrastructure); APS Pharma (Germany, infrastructure)
SpePharm (Netherlands)	Pan-European marketer of hospital/specialist products	
Amdipharm (part of supply firm Waymade Healthcare PLC)	UK and European channels for selling undervalued assets in areas such as palliative and critical care	

Product-Focused

COMPANY NAME	THERAPEUTIC AREA FOCUS	LATEST PHASE
Circassia (UK)	Allergy	Phase II
Neuropharm (UK)	CNS	Phase III
Nitec Pharma (Switzerland)	Chronic inflammation	Phase III
Santhera Pharmaceuticals (Switzerland)	Neuromuscular diseases	Phase III/filed

SOURCE: Company reports, Windhover's *Strategic Transactions Database*

The Infrastructure-First Model

Specialty European Pharma Ltd., founded in September 2006 by Advent Venture Partners, falls in the second category. It plans to acquire late-stage or marketed specialist drugs and sell them to a targeted group of European prescribers, building up an infrastructure in the top five countries and possibly beyond. "We have honed in on this notion of identifying clearly defined groups of prescribers, and are now finding products to fit

that framework," explains Patrick Lee, general partner at Advent.

SEP found two in February 2007, in conjunction with a €15 million (\$19 million) financing round. [W#2007300073] The product profiles typify the kinds of assets a young, commercially focused spec pharma must settle for—distressed drugs with a troubled regulatory history, products that are too small to have triggered widespread interest, and/or assets that are not marketed outside a developer's home market, or are not widely available across Europe, for whatever reason.

Haemopressin (terlipressin) is marketed in a handful of European and Asian countries for bleeding oesophageal varices, a condition associated with severe liver diseases. SEP accessed this product by acquiring Swiss-based **Proreo Pharma AG**, which "didn't have the scope or ambition to be pan-European" itself, notes Lee. *Haemopressin*, an old product that sells €3–4 million, wasn't big enough for consolidating mid-sized European drug firms such as **Merck Serono SA** (part of **Merck KGAA**) or even regional firms such as Spain's recently listed **Laboratorios Almirall SA**, "but it makes sense for a SEP," explains Lee.

So, apparently, does prostate cancer drug abarelix (*Plenaxis*), to which SEP acquired worldwide rights from **Praecis Pharmaceuticals Inc.** shortly after it became part of **GlaxoSmithKline PLC**. [W#200720117] [W#200610223] Praecis had previously tried but failed to sell off *Plenaxis* in the US: the drug had been through several partners on both sides of the Atlantic, and eventually gained FDA approval in November 2003 for a subset of patients with advanced prostate cancer. *Plenaxis* was also approved in Germany in 2005, but Praecis didn't have the resources or expertise to market it in Europe (and partner Schering AG, now **Bayer Schering Pharma AG**, had by then dropped out). [W#200420318] [W#200610040]

SEP thinks it can do what Praecis couldn't: gain wider approval for the product across Europe, market it, and make money from it. The European label is more advantageous than that in the US; German authorities passed it as a first-line therapy, in patients with advanced or metastatic hormone-dependent prostate cancer for whom androgen suppression is appropriate. "We understand the regulatory processes at play in Europe, and can demonstrate that to partners," argues Geoff McMillan, SEP's founder and CEO, who was involved in building Elan's European and international businesses prior to its sale to Apax.

SEP has indeed since acquired German, French, and Italian rights to *Amphocil* from **Three Rivers Pharmaceuticals LLC** and a diagnostic product called *Cortirel*, approved and marketed in Germany. It's a mixed bag of products, but it's a start. "We have to be pragmatic and must build the company around the products that we acquire," McMillan told *IN VIVO*.

And that's the problem, say critics, with some of these new spec pharma hopefuls. "They're trying to give substance to a shell, run some financials, and make it look like an attractive pharma company," says one. "It's all window dressing; they're just looking for a quick exit." In SEP's case, the exit part, at least, is right: "The goal is to do just as Apax did with Zeneus. Apax's return and time frame are reasonable and reproducible," insists Lee.

Easier Said than Done

But building spec pharma in Europe is a slow business—especially one with a sufficiently broad, yet efficient and integrated infrastructure, and the right products, to attract a buyer. Zeneus began with a head-start: Elan had previously taken five years to build its European business; that's why it was such a valuable asset for Apax and, later, for Cephalon. (See "*Medeus: How to Find & Buy a Ready-Made Euro Infrastructure*," *In Vivo Europe Rx*, April 2004 [A#2004600044].)

Others already on the spec pharma trail have discovered just how long it takes. **Archimedes Pharma Ltd.** was set up in late 2004 by Richard de Souza, previously director, international at Shire, with backing from private equity firm Warburg Pincus. [W#200410284] Like SEP, Archimedes aims to become an attractive

partner for launching products across Europe, and to quickly reach profitability. The plan was to get a footprint in one or more of the top five markets in Europe through acquisition (a feature of most if not all spec pharma growth), build on top of that base, license in pan-European product rights, and then add a development organization to supply in-house drugs. (See "Ex-Shire Team Builds New Euro-Specialty Group," IN VIVO, March 2005 [A#2005800049].)

But the plan is stretching its time line. Archimedes only just secured its first significant piece of commercial infrastructure in November 2006 when it acquired UK-based **Link Pharmaceuticals Ltd.** [W#200610188] "There used to be [buying] opportunities from Big Pharma selling units or tail-end drugs," recalls de Souza. That's dried up, he says. When large companies do spin out assets, the process tends to be driven by an internal champion and result in a stand-alone company—often with its own downstream aspirations. So acquisitions, he argues, will more frequently come from smaller, independent companies in Europe, many of which are private owned and difficult to assess and buy. "You need relationships. It took two and a half years to get Steve [Mountain, Link's CEO] to the table," he admits.

Still, Link came with about \$30 million in revenues, a solid organization in the UK, and start up operations in France and Germany. And its products fit with Archimedes' focus on pain. They include newly launched *Gliadel*, a biodegradable wafer impregnated with an anti-cancer drug, carmustine, for high-grade glioma licensed from US spec pharma **MGI Pharma Inc.**, *Metastron*, a radio-pharmaceutical for bone-pain associated with prostate cancer, and sustained-release morphine *Zomorph*. De Souza has reorganized Link's sales and marketing operations, trebled the sales force, and has France and Germany operating at about the \$5 million mark.

This is still small (Zeneus is thought to have brought an additional \$100 million in sales to Cephalon). But Archimedes' size makes it easier to chalk up tremendous growth—like the 20% de Souza claims for the UK business. And that appeals to Warburg Pincus managing director Nick Lowcock. He knows he won't get a quick exit—Warburg Pincus has held its other spec pharma investments, including **Wyeth** delivery offshoot **Eurand NV** and **ProStrakan Group PLC**, for seven years or more. [W#199930521] For Lowcock avoiding acquisition fever is more important than speed. "The worst mistake is to mess up the potential to make a lot of money by paying too much for something that's not great," he says.

ProStrakan's Focus Challenge

"Stay focused" is another good piece of advice for aspiring pan-European spec pharma, if ProStrakan's experience is anything to go by. Founded in 1995 by Shire's creator Harry Stratford, ProStrakan is another Shire wannabe. But the group's apparent lack of focus—its acquisition trail has left it with 40 or more products, across a range of therapeutic areas, and included an overambitious foray into early R&D—is the most likely reason, say critics, for its lackluster valuation. The group's shares have lost a third of their value since listing in 2005; the company is now worth less than the \$300 million or more it has raised since inception. Investors—including Warburg Pincus, which owns 36% of the equity—are still waiting for ProStrakan, whose current turnover is just under \$80 million, to turn a profit. "There's nothing wrong with the model per se," notes a former employee, "but it's best to keep it simple, and not have too many products."

But although everyone agrees on the virtues of focus, this isn't always easy to achieve for young groups under pressure to hit turnover and margin targets. "One has to be able to afford a focus," says Wilson Totten, PhD, ProStrakan's CEO and previously head of R&D at Shire. "One can't afford to be too choosy," he continues.

Now, though, Totten claims focus is coming, in particular on oncology supportive care, and in urology and endocrinology. The company has divested some products deemed too small, like acne treatment clindamycin (*Zindaclin*), he explains, and is trying to move into higher-growth products differentiated on therapeutic benefit, not just price. The company attracted *Rapinyl*, a muco-adhesive flash melt fentanyl for breakthrough cancer pain, from Sweden's **Orexo AB** "because we're one of the few companies that can sell throughout

Europe in one transaction," claims Totten, although the group has since brought Orexo back in to a joint venture in the Nordic countries. [W#200520786] [W#200720539] ProStrakan also has worldwide rights to two drugs from **Cellegy Pharmaceuticals Inc.**: testosterone gel *Tostran* for hypogonadism, and glyceryl trinitrate (*Rectogesic*) for anal fissures. [W#200620625] It's boasting four potential pan-European launches over the next 18 months.

In theory, with its established European presence, improved focus, and low valuation, ProStrakan could make an attractive takeover target. The snag: it won't be profitable before 2009 at the earliest (and also has a \$100 million debt facility, taken on in March 2007). US-listed spec pharma are valued on an earnings basis, and they won't want to make a dilutive acquisition.

Europe Is Not Enough: Transatlantic Virtues

By then, though, ProStrakan hopes to have its own US revenues: after long negotiations, the firm last year expanded what began as a European-only deal with Cellegy to include North American rights to *Tostran* and *Rectogesic* (where they're branded *Fortigel* and *Cellegesic*). Taking on a new market looks odd for a group with no track record or competitive edge there—it will rely, even more so than in Europe, on distressed assets like Cellegy's, both stalled at FDA and Cellegy couldn't afford the extra trials.

On the other hand, the US is the only market where spec pharma in any flavor appears to have created significant sustained value (with the possible exceptions of **Nycomed Group** or Sweden's **Meda AB**, neither of which are strictly specialist and both of which now have US operations thanks to acquiring **Altana Pharma AG** and **MedPointe Inc.**, respectively). [W#200610153][W#200710107] The US is what made Shire big—the seeds of its extraordinarily successful *Adderall* franchise came via two US company acquisitions, Richwood Pharmaceutical Co. Inc. and Pharmavene (now **Supernus Pharmaceuticals Inc.**), and the US has long accounted for the vast majority of Shire's sales. [W#199710142] [W#199710049]

That's why spec pharma entrepreneur Bryan Morton's latest venture has started out transatlantic from day one. Morton, who was CEO of Zeneus until shortly before its acquisition by Cephalon, is founder and CEO of EUSA Pharma, launched in May 2006 with \$53 million in combined A and B round funding from VC firm Essex Woodlands. Morton felt he'd done only half the job at Zeneus, caught short by an investor keen to make a quick return before the company had cracked the really valuable market. "Zeneus was bought because it was a strong European company; but we could have done this six times over and sold for even more," he declares.

Apax had invested in Zeneus from a variety of older funds, some of which needed the return rate boost that could be provided by a quick and lucrative exit opportunity. This time round, Morton has ensured he accesses brand new funds—Essex Woodland's freshest, seventh fund, with nine years to run, where there's less pressure on keeping the ROI numbers up. "There's more value over the long term in building a transatlantic company than just doing another Zeneus," confirms Petri Vainio, managing director at Essex Woodlands in London.

He knows just how much: Essex was an investor in Richwood before it was acquired by Shire. "We've seen the movie once already," says Vainio, and EUSA's blueprint is the same: like Shire, to build a foundation of European infrastructure with rapid revenue growth, driven in part by a US presence. EUSA even has, as chairman, Rolf Stahel, the CEO who grew Shire to a \$3.2 billion company in nine years.

But so far, Shire's success has been unique. Most classic spec pharma are geographically concentrated—either in the US, parts of Europe, or, increasingly, in Japan and even China. (*See Sidebar.*) Outside the US, the geographic focus is part of the competitive edge in attracting drugs. Usually, it's only when they've become too big for their home territories that companies expand beyond.

A notable exception among smaller groups: **Pharmion Corp.**, a US-headquartered specialty pharma focused on oncology and hematology with half of its sales in Europe. (See "*Pharmion Bets that Europe is Alright for Some*," START-UP, *January 2004* [W#2004900009].) With revenues approaching \$250 million and a \$1.4 billion market cap, Pharmion has access to the world's two largest markets but also added flexibility—it can license US-only in its areas, but also EU-only and global rights (its US and EU selling organizations are entirely separate). [W#200330358] This allows it to hedge risk, too: Pharmion is the EU (but not US) partner for **GPC Biotech AG's** prostate cancer candidate satraplatin, recently rejected by FDA, and it was insulated from the worst of the sell-off that hit GPC. [W#200520765]

And there's another advantage to having foot in both camps from day one: it forces focus on just a handful of therapeutic areas. In the US, spec pharma have to be focused in to attract products, both because of the more significant competition and because specialists tend to work out of individual practices across the country. In Europe, most specialists work alongside each other in hospitals. That means firms can leverage sales forces across various disciplines, cost-effectively—and they must, to some degree, because the country markets are smaller and tougher, so a single product will be less profitable. But this also means that "it's easier to be de-focused in Europe," adds Vainio, "and some have fallen into that trap."

Pharmion's experience shows that it's possible to get the best of both worlds by balancing focus, driven primarily by the US market structure, with sufficient leverage in Europe. Morton thinks EUSA's chosen specialties—critical care, oncology, and pain—will mean it can do the same. "We picked our areas in part based on an analysis of how well FDA and EMEA have historically dealt with products in these fields," he adds, and on the basis of his team's experience. It wasn't, he claims, a case of building a company around whatever product it already had. "You need a core skill," he continues, because the ultimate goal is to be a very strong sales force with a range of target customers.

EUSA's moved beyond the talk: the firm has five marketed products (including one in the US) and over half a dozen in the pipeline, via three acquisitions. The first came through a merger, at inception, with private Talisker Pharma, which had EU rights to *Rapydan*, a rapid-onset anaesthetic patch marketed in the US as *Synera* by **Endo Pharmaceuticals Holdings Inc.** The next target was French, VC-backed **OPI Group**. [W#200710031] At first glance this wasn't an obvious target: research-based OPI had a couple of clinical candidates and one in preclinical, two marketed drugs in onco-hematology, and just a dabbling of commercial activities. But the fact that OPI had not set up extensive country organizations was an advantage—it meant EUSA could avoid the cultural integration challenges and cost-cutting, and instead use its own infrastructure to exploit OPI's customer contacts and systems. Those were working well; "OPI had excellent direct sales into hospitals and was growing quickly," notes Morton. Critically, too, OPI had US rights to its drugs.

Others spotted OPI's potential—and assets—too; it was a highly competitive auction that Morton moved fast to secure, helped by a \$175 million second round, led by Essex and 3i—which will fund EUSA to profitability, according to Vainio. [W#200730137] Late in August, EUSA announced its third acquisition, of critical care and pain control products plus a pan-European sales and marketing infrastructure from **Innocoll Pharmaceuticals Ltd.**, a division of **Innocoll Inc.** [W#200720586] The deal brings EUSA a direct presence in more than 20 European countries, *Collatamp G*, a marketed implant that offers site-specific delivery of the antibiotic gentamicin for postsurgical acquired infection, and two late-stage candidates. EUSA also has first rights of refusal on US rights to two of the assets in the agreement.

As a result, Morton expects by year-end to have a European infrastructure equivalent to Zeneus' and to be building up in the US. But, he cautions, "this isn't a 22-month exit play. It will take a lot longer." By sticking to its therapeutic area focus, divesting non-core assets and concentrating on just a handful of drugs in the \$50–\$300 million range, Morton hopes to build a group worth \$1 billion within three to seven years. "We're doing transatlantic spec pharma, not necessarily bigger than Shire, but better," he says. As for the uncharacteristically broad geographic focus, that means "we're really more like specialty Big Pharma."

Products Trump Infrastructure

Still, regardless of how, where, and how fast the new generation of European spec pharma build their businesses, in the end their success—and their attractiveness to potential buyers—will depend less on commercial reach than on products.

Sure, Cephalon's acquisition of Zeneus was largely about infrastructure—taking it beyond France, where it had already acquired Groupe Lafon, creator of its star drug substance modafinil (sold as *Provigil* for excessive daytime sleepiness), into the top five markets. [W#200110233] But the deal was also about oncology assets. "Zeneus had [liposomal doxorubicin] *Myocet* and [amphotericin B] *Abelcet*," explains Alain Aragues, president, Cephalon Europe. They fit with Cephalon's new, expanded therapeutic-area focus and pipeline candidates. As products become more hotly contested, "it will become tougher and tougher to create another Zeneus," opines Aragues, who was involved in integrating both Lafon and Zeneus. "You need not only infrastructure, people, skills, and experience, but also interesting products."

Peter Lankau, CEO of Endo, is even more forthright: "Products come first, infrastructure second," he declares. "We wouldn't be interested in a pan-European infrastructure for infrastructure's sake, unless the portfolio justifies a long-term investment in Europe, and the products offer opportunities both in the European and US markets."

This drive for products is what's inspiring investors behind another breed of spec pharma, prevalent on both sides of the Atlantic, whose philosophy is to start with a mid-to-late-stage, highly focused pipeline that's designed to be fully marketable with a specialist sales force—but for which the infrastructure doesn't exist yet, and which, in fact, it may never build. "In Europe, we've tended to start with assets to attract experienced management and build the necessary infrastructure in a cost-effective way," notes Zina Affas, principal at VC firm Atlas Ventures in London.

The assets, generally with low innovation risk, may come from anywhere. Swiss-based **Nitec Pharma AG** has worldwide ex-German rights to a now-filed, modified release version of an anti-inflammatory drug from Merck KGAA and an option on at least one more, spinout style. [W#200430766] CNS-focused **Neuropharm Group PLC** is working on a reformulation of generic fluoxetine for autism, hoping to create a market in this virtually un-treated condition, similar to what Shire did in ADHD or Cephalon in daytime sleepiness. Run by Robert Mansfield, previously CEO of Vernalis Group PLC (which, with two marketed drugs, is one of Europe's many biotech-spec pharma hybrids), Neuropharm has orphan drug status for its two lead candidates and its commercial ambition is entirely US focused—all factors that helped it raise almost £20 million in its AIM IPO in London in March. [W#200730143]

Or the assets may come out of universities, where maturing and better-funded tech transfer divisions are increasingly able to take compounds further downstream. Steve Harris, formerly CFO of Zeneus and who took over from Morton as CEO prior to the Cephalon sale, now runs **Circassia Holdings Ltd.**, which has a pipeline of allergy treatments targeting the immune system, including one that has completed Phase II. Seeded by Imperial Innovations, the tech transfer arm of Imperial College, and with two technology platforms and a pipeline that stretches back to preclinical, Circassia looks more like a biotech spinout. Other modern spec pharma have R&D capabilities, too, which their investors position as a guarantee of future product supply, not a risky drain on finances. But "this is spec pharma," argues Harris, at least since the first funding round in January 2007. "Our intent is to build a business with products that we will commercialize ourselves to allergy specialists with a focused sales force, and any products we develop or license must fit that profile."

European spec pharma is still fundamentally about lowered risk, and about selling or intending to sell drugs. But the point is that these firms' products aren't always (or indeed often) the approved, undermarketed assets that spec pharma used to live off. Infrastructure is for later, not now. "The [spec pharma] term is badly mis-used," opines Domain Associates' general partner Jim Blair, "to describe those with an

acquire—and—market strategy." That definition is out of date, he argues. Nowadays it's far more capital efficient to buy products in mid—to—early clinical development, as they're much cheaper than marketed drugs.

It's also possible to make lots of money from them before they've even got anywhere near the market because late-stage products with little or no added cost structures are just what Big (and mid-sized) Pharma will pay high prices for. Domain Associates, in the US, has shown how this model works, most recently building **NovaCardia Inc.** on two in-licensed drugs, then selling one drug and the company to **Merck & Co. Inc.** for \$350 million and starting another company around the second drug. [W#200710111] (*See "NovaCardia & Domain: New Model Spec Pharma Investing," START-UP, September 2007 [A#2007900157].*) Not all of these new-style spec pharma will be acquired, but that's why building in the marketing-focused option, at little or no extra cost, makes sense: it provides a viable alternative future if the right trade exit doesn't present itself.

Betting on the Commercialization Gap

Unless they all get snapped up, the product-first spec pharma may provide significant competition for the infrastructure-focused lot because as well as marketing (or intending to market) their own drugs, they'll also be looking to in-license supplementary assets, in a similar size-bracket, to justify building that infrastructure. It's also still fashionable among biotechs to hang on to product rights, and mid-sized and larger pharma are now competing in some specialist areas. All the while, most Big Pharma still hate to out-license tail-end or de-prioritized assets. Thus ProStrakan, SEP, EUSA, and others trying to support an infrastructure need to question whether and at what cost product supply, through license or acquisition, will continue. "There are many more ways for small companies to commercialize their own assets now than there were five years ago," points out Atlas' Affas.

But there are also many more challenges for small companies intending to approve and commercialize their own drugs. A toughening regulatory environment has already tripped up smaller firms trying to get to market alone. Shares in GPC, one of Europe's discovery-platform turned specialty plays, fell 70% after the satraplatin snafu, and CEO Bernd Seizinger, MD, PhD, afterward suggested the company may have to bring in a US partner after all. Noting similar regulatory hiccups at other firms, including **Dendreon Corp.**, some analysts have begun to suggest a possible FDA bias against smaller biotechs with one-trial submissions. (*See "Satraplatin's Stumble: Is Accelerated Approval Under Threat?" this issue [A#2007800134].*) It's also long been clear that the vast majority of co-promote clauses written into today's deals—giving biotechs the option to share commercialization with a larger partner—fail to turn into reality. (*See "Co-Promotes: A Marketplace Reality, But Do They Make Sense?" IN VIVO, April 2007 [A#2007800060].*)

As the costs and risks associated with commercialization become clearer, and as prices for even proof-of-concept stage assets rise, the product-focused spec pharma, particularly those that have retained significant R&D capabilities, may decide to stick to development. That's exactly what Innocoll did, declaring it would focus on development as it sold its commercialization infrastructure to EUSA. "We're betting on that commercial gap—taking products through registration and onto the market," sums up Morton. Many of the companies wanting to hold onto US rights "don't have a clue how to commercialize drugs," he asserts. They're already looking to sell off European rights, which is why EUSA wants to build a European infrastructure. But "we're also saying that there's a better way: 'think about a one-stop transatlantic deal, with your product as our main interest.'"

"It's still possible to build a European Cephalon," contends Circassia's Harris; Warburg Pincus' Lowcock, too, reckons the model still has value in Europe. Perhaps it does. But judging from the new flavors of spec pharma being created, simply building a European infrastructure won't cut it. Zeneus may remain an inspiration, but it was also an exception. As one US spec pharma business development director points out, "one successful private equity exit does not a sector make."

Spec Pharma Comes to Japan and China

While Europe struggles to find its spec pharma feet, the model is spreading to other large yet hard-to-access markets like Japan and China. It's early days, but old-style spec pharma—buying approved drugs to sell into a new market—may yet prove easier to replicate in these single markets than in fragmented Europe.

There are now at least half a dozen Japan-focused spec pharma firms. Some, like **SymBio Pharmaceuticals Ltd.** or newly created **JapanBridge Inc.**, license late-stage or approved US or European drugs for Japan (where many remain unavailable), and others like **Artisan Pharma Inc.** are doing the reverse, mining Japanese pharma firms' pipelines for assets they can develop, register, and sell elsewhere. (*See "Specialty Pharma: Tapping Japan," IN VIVO, January 2007 [A#2007800005].*)

And now China's following suit. **NovaMed Pharmaceuticals Inc.**, which secured \$5 million from Atlas Ventures in July 2007, has already assembled a range of late-stage or approved products—including a tail-end drug from **Sanofi-Aventis**—which will be marketed in China via its 100-strong sales force. In China, as in Japan, "knowing the right people really matters a lot," according to NovaMed board member Zina Affas, a principal at Atlas Ventures. So does knowing the system: in China, for instance, drugs must first be listed at individual hospitals before they can be sold to prescribers there. NovaMed's co-founders are Mark Lotter, who built **AstraZeneca PLC's** Chinese sales force, and Bo Shao, a Chinese entrepreneur.

Private **RHEI Pharmaceuticals Inc.**, based in New Haven, US, also has its sights set on China and neighboring markets, for which it's in-licensing in assets in cardiovascular disease, oncology, and infectious diseases. The company last year licensed controlled release aspirin *Asacard* from **Flamel Technologies SA** and a Phase III compound from **AP Pharma Inc.** for chemotherapy-associated nausea. [W#200620306] [W#200620649]