

# From outsourced to open: the continuing evolution of the drug discovery business model

One doesn't have to look far to find that the large pharmaceutical business model has many market forces working against it, such as patent expirations, dwindling pipelines, and reduced R&D productivity. However, these factors are driving smaller organisations and individuals to take on small molecule and biological drug development, sometimes with great success.

**V**irtual drug discovery entrepreneurs, armed with their experience, personal networks, online tools, and countless contract research organisations (CROs) who will manufacture and test their drug candidates, have shown that drugs can be developed outside the confines of traditional biotech and pharma. This movement has in turn sparked a more open approach to the development of medicines, which is being embraced at all levels of the industry. Examples of virtual and open discovery organisations from the San Diego region, where the author resides, are highlighted in this review, as well as those from other regions as needed.

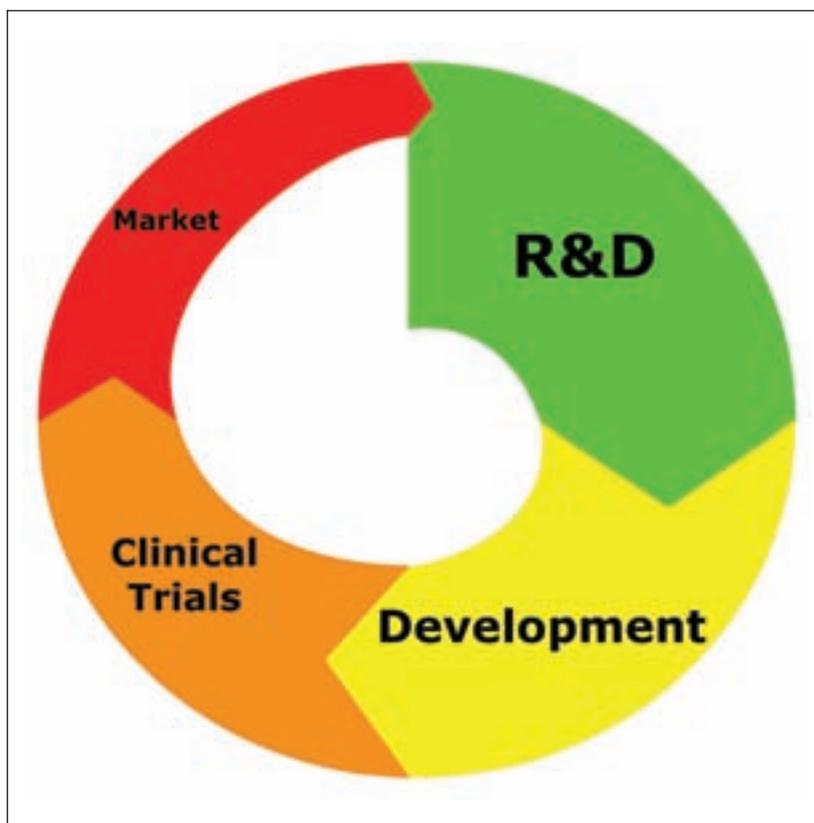
As far as failing business models go, Pharmaceutical companies could arguably be placed in the same category as airlines, as we are no longer surprised to hear of major cutbacks or other signs of distress. The 2011 CMR International Pharmaceutical R&D Factbook<sup>1</sup> indicated that while drug sales are increasing, only 5% are from products launched in the last five years. Of the 21 NMEs launched in 2010, down

from 26 in 2009, only one-third were from larger companies. This downward spiral will continue as R&D expenditures reached a three-year low. The Fitch Global R&D Pipeline reports for 2011 indicated that acquisitions, not internal R&D, are driving the pipelines of big pharma and that 2012 may be the most challenging year for them due to different forces, most notably a cascade of patent expirations<sup>2,3</sup>. Although the success rate for in-licensed compounds is on average 20% lower than those developed in-house<sup>1</sup>, they are desperately needed to fill Pharma's dwindling pipeline. As shown in **Figure 1**, the dearth of marketed drugs leads to fewer financial resources for R&D which will result in an implosion unless their business model is changed.

What factors are leading pharma on this downward spiral? A 2008 Harvard Business Review (HBR) article<sup>4</sup> sheds light on the 'success-seeking' behaviour of large pharma. Negative information is ignored, or the correct experiments aren't done in the first place due to the fear of not succeeding. Smaller or virtual companies succeed by becoming

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**Figure 1** the anti-pharma, by building a culture in which the experiment is more important than the success of the programme. The HBR article details the success of Chorus, a 22-person company spun out of Lilly whose goal is to evaluate compounds quickly and autonomously. By choosing smaller scale, ‘killer’ experiments, Chorus has made go/no go recommendations resulting in a 3-10 fold ‘productivity enhancement’<sup>5</sup>. Chorus was also able to make its decisions in a capital-efficient manner by utilising contract research organisations (CROs) in an ‘a la carte’ fashion rather than continuously staffing resources.

The wide selection of drug discovery CROs is one of the major drivers of small and virtual company success. Kevin Lustig, CEO of Assay Depot, an online CRO marketplace, indicates that it has 6,491 CROs in its directory (Figure 2)<sup>6</sup>. Those who are concerned about job loss in the countries where many drug discovery scientists are trained should note that the majority are in the US and Europe. The Assay Depot directory enables small companies by providing a wealth of information about the drug discovery process, as CROs are smartly categorised as being in Biology, Chemistry, DMPK, Pharmacology or Toxicology, with more detailed subgroups. The goBalto direc-

tory also includes clinical research organisations and related businesses and lists more than 16,000 entities. These portals provide easy access to information, ratings, and even ordering and managing outsourcing. Additionally, outsourcing partners can be found through networks such as LinkedIn, either through personal connections, searches, or groups (there are even several LinkedIn groups dedicated to outsourcing). Conferences such as the Biotechnology Industry Organisation annual meeting and EBD Group partnering events have developed online applications to facilitate meetings between pharma and biotech collaborators, although the emphasis is normally on later stage partnerships.

Virtual drug discovery programme managers are often veterans of the industry and rely heavily on their own networks and experience to get the work done. Jim Hauske, founder of Sensor Pharmaceuticals, spoke about forming his virtual R&D network at a July 2011 event held by the San Diego Biotechnology Network (SDBN)<sup>7</sup>, describing 10 companies he outsources to as his ‘collaborators.’ Hauske’s talk was followed by a panel of experts from both sides of the outsourcing fence, and they reiterated this need to work closely.

Are most teams truly virtual, in other words do geographical differences matter at all? At the SDBN event, the consensus was that only barriers to working with companies in different regions were time zone differences. Normally, meeting in person near the beginning of the project is desired, but not essential. Indeed, CRO services have become so all-inclusive that Sensor’s Hauske said that he’s developed assets in which he’s never actually held a vial of a compound. The availability of video conferencing applications for individuals and small companies, which adds the human connection to a collaboration, allows meetings to take place across time zones. To manage projects, collaborative software such as SharePoint allows for secure file sharing and project management. More recently, Collaborative Drug Discovery introduced a web-based drug discovery data management product called CCD Vault, which is more affordable than the enterprise systems larger companies use. It has been suggested that IT advancements are the key to streamlining the drug discovery and development process, and Chorus’ planning and management application ‘Voice’ is touted as being integral to their success.

While these companies can be 100% virtual in theory, there are benefits to looking locally for collaborators, including closer communication and

reagent or equipment exchange. In San Diego, our biotechnology network is one of several grass roots organisations facilitating networking in the region, with 6,500 connected via a LinkedIn Group. The San Diego Entrepreneurs Exchange (SDEE) was founded in 2009 and holds bimonthly meetings attracting 100-200 biotech professionals interested in the success of biotech business in the region. They've also created an online 'incubator' in which laboratory resources can be listed for rent or sale. San Diego's regional hi-tech/biotechnology development group CONNECT has also initiated a 'Near sourcing' program which helps companies meet their outsourcing needs locally.

Who starts a virtual company, and how? Jim Hauske outlined five requirements for starting a successful virtual drug discovery company at our event in San Diego:

- A novel idea
- Someone else's money
- Operational and deal making experience
- Experience raising money
- An extremely thick skin

Hauske was too modest to mention that he has the right provenance for the job, which likely made his pathway successful. Finding and evaluating an idea as novel and potentially successful, and the wisdom that leads it from concept to asset requires expertise that few possess. Hauske was involved in the development of Zithromax at Pfizer, and after further experience managing projects and outsourcing at Sepracor, has become a serial entrepreneur. He has licensed technologies and small molecule clinical candidates through three of his companies, and his current company Sensor Pharmaceuticals focuses on treatments for metabolic and cardiovascular disorders.

Virtual drug discovery is by no means limited to the development of small molecule drug development, as CROs who develop and produce antibodies and biologics continue to become more plentiful and experienced. Assay Depot lists more than 670 antibody services providers in its directory, and more than 400 services (not all that are listed as vendors also list their services). San Diego's BioAtla leverages an antibody and other protein production sites in Beijing to cut costs, and works on either a collaborative or project by project basis. In addition, BioAtla is in tune with current intellectual property (IP) procedures and regulations, and helps its clients successfully navigate them, without laying claim to them. BioAtla has worked closely with Fenta Pharmaceuticals, a

San Diego-based virtual company, resulting in an IND filing in August 2011. This is a limited example but in essence, any pre-clinical or clinical activity, is available on an out-sourced basis. Entrepreneurs that can develop the proper network are able to accomplish exactly what a classical biotech or pharma company can in terms of drug development.

Recently, the returns on a few virtual companies cannot be denied. One recent example from the antibody space was the sale of Stromedix to Biogen Idec for a Humanized monoclonal antibody to integrin  $\alpha v \beta 6$  being developed for idiopathic pulmonary fibrosis. The deal was extremely valuable with \$75 million as an upfront payment and subsequently backed with a total of \$487.5 million in potential milestones. The development of the Stromedix product was totally on a virtual basis and the exit was on par with peers structured as a classical company.

That said, one of the biggest challenges faced by virtual companies is finding funding in the first place. As Hauske pointed out, he used his own money initially, but indicates this strategy is not optimal. Many small biotechnology companies are relying on creative sources of funding such as small business innovation research (SBIR) grants. Scott Struthers, Founder & CSO at Crinetics Pharmaceuticals and member of the SDEE organising committee, said "The NIH SBIR programme has long been a crucial driver for company creation in the biotech space. In the last few years, its role has become increasingly important as early stage funding from traditional venture capital (VC) sources continues to dry up." This funding allows small companies to initiate projects leading to growth, albeit slow compared to that achievable with VC funding. We've all seen VC funding being used frivolously however, and perhaps this slow growth is necessary for effective drug discovery. Patient advocate groups, such as the Michael J. Fox Foundation for Parkinson's Research, seem to have found a good blend of providing targeted funding while fostering collaboration between teams.

Creative financing can cross over to CROs as well to enable virtual drug discovery. For example, Seattle-based Emerald BioStructures is a key partner with the Seattle Structural Genomics Center for Infectious Disease (SSGCID). Working within the consortium, Emerald has solved the 3D structures of more than 450 novel infectious disease target proteins since the start of the programme in 2007 to enable the pharma and biotech industry in the development of new antibiotics. The need to

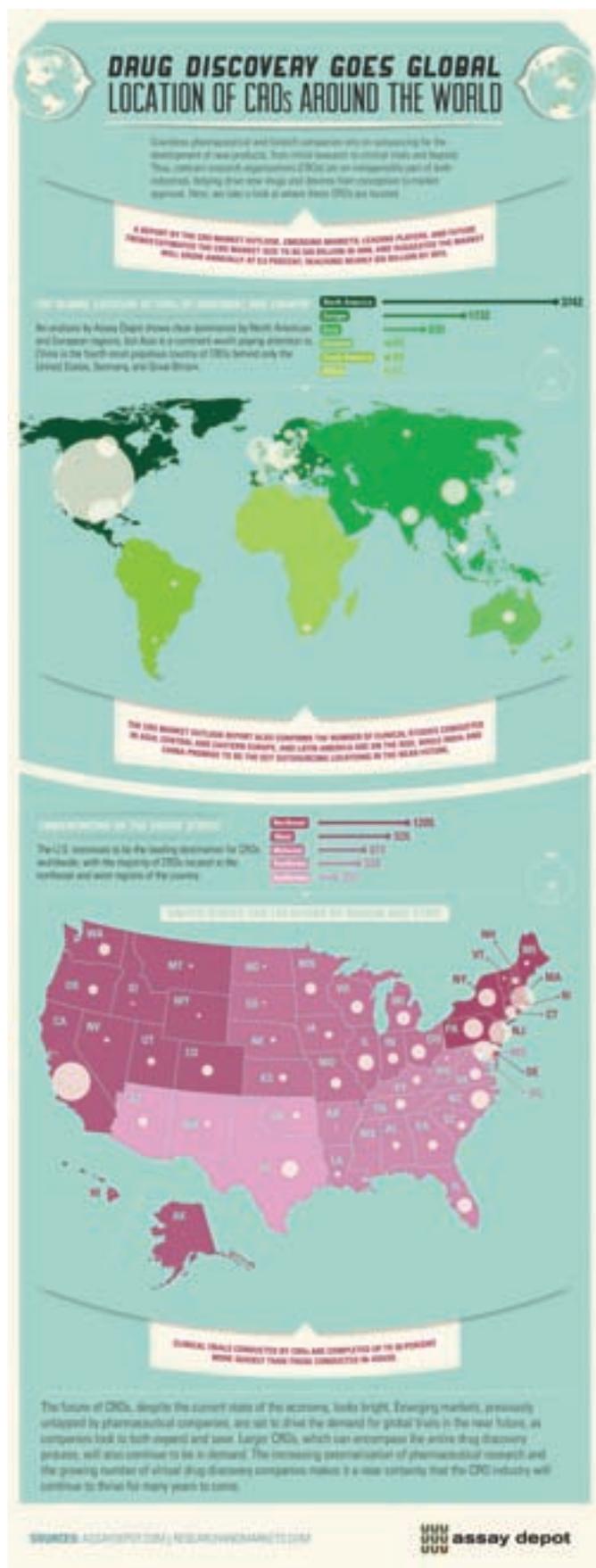
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**Figure 2**



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The fact that Lilly's three negotiated deals are with academic institutions, rather than biotech companies, also represents the momentum of the translational research movement, which has been partly fuelled by pharma R&D scientists who returned to academia and the growth of strong university core resources. Peter Schultz, long time San Diego entrepreneur and faculty member of The Scripps Research Institute, has announced the formation of the California Institute for Biomedical Research (Calibr) with \$90 million funding from Merck. Calibr will perform early stage research at 'arm's length' from Merck, and Schultz commented to Xconomy<sup>10</sup> that collaboration will be much easier with this non-profit. As with Chorus and Inception Sciences, it appears Pharma needs to get 'out of its own skin' to perform drug discovery more effectively.

Pfizer and Johnson & Johnson also support drug discovery incubators in San Diego, and while it appears the former appears to be ramping down, J&J's Janssen Labs is taking off, launching in January 2012 with some fanfare. The 30,000sq ft space is described as a 'no strings attached' facility where start-ups can use facilities in a modular manner, expanding to using more when needed. The space is meant to foster 18-20 companies, and J&J will take no equity in them and states that they truly are creating the incubator to 'fertilise the soil' for the drug discovery industry as a whole<sup>11</sup>. Besides the great PR that the company will receive from this endeavour, it is likely that they will benefit down the road from an influx of new ideas and perhaps a talent pool.

### An 'extreme' version of open drug discovery

The virtual drug discovery paradigm has shown a path towards the development of new medicines through increased collaboration between increasingly experienced individuals and organisations. An open model is the next progression and promises to shed even more light on the path to a successful drug. The virtual model is not without critics who say that drug development should not be relegated to VCs who may be taking random 'shots on the goal' in financing 'throwaway' biotechs<sup>12</sup>. Similarly, the open model may face criticisms as it evolves, as complications with intellectual property and later stage funding will likely emerge. Soon the success rate of these assets in the clinic will be assessed, at which point we'll be able to fully judge the progress.

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