

Outsourcing lead optimisation – the quiet revolution

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The outsourcing of lead optimisation services is a relatively new but growing market. Historically, pharmaceutical companies have been hesitant to outsource activities at the lead optimisation stage of the drug discovery process, but more recently this reticence has largely been put aside. As a result, a growing number of companies with diverse backgrounds and geographical locations are now competing to offer services in this sector. Currently, a particularly significant trend is the move towards 'off-shoring', which promises to drive further changes in this rapidly evolving market in the near future.

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▼ Historically, the pharmaceutical industry is no stranger to outsourcing. According to Cavalla [1], industry-wide outsourcing in pharmaceutical development (normally defined as the phase between candidate identification and market) is estimated at 30–35% and is continuing to grow. In specific development areas, such as toxicology, the percentage of outsourced services is even higher. However, pharmaceutical companies have only recently considered outsourcing at earlier research stages in drug discovery, for example, between target identification and candidate identification [perhaps with the exception of sending compounds for selectivity screening at companies such as CEREP (<http://www.cerep.fr>)]. Lead optimisation is a particularly time- and resource-intensive stage of drug discovery during which a compound that shows some effectiveness against the biological target of interest is converted through many iterative steps into a drug candidate. To quote from a recent market research report – 'Five years ago, nobody would have considered outsourcing these [lead optimisation] services. Now, virtually every major pharma is doing it' [2]. The same report estimates that the market for outsourced lead optimisation services was worth US\$1.63 billion in 2003. This figure is projected to increase more than

twofold over the coming years to generate a market of US\$3.53 billion in 2007 [3].

This review focuses on the market for outsourced lead optimisation and discusses the traditional reticence of the pharmaceutical industry regarding lead optimisation outsourcing and the driving forces behind the change in attitude towards outsourcing in recent years. The current state of the market for lead optimisation outsourcing will be examined and profiles of the companies that are active in this sector will be used to highlight some of the current trends in what is a highly dynamic and rapidly evolving arena.

Outsourcing lead optimisation

For the purposes of this review, lead optimisation is defined as those activities that are required to optimise a screening hit to a pre-clinical candidate. Thus, lead optimisation invariably comprises synthetic and medicinal chemistry, biochemical and functional screening, computer-aided drug design, *in vitro* and *in vivo* pharmacokinetic studies and physicochemical (e.g. solubility, partition coefficient and acidity) studies [4]. Until recently, the outsourcing of these activities was rarely (if ever) considered by major pharmaceutical companies, although for some biotechnology companies outsourcing might have been the only option for progressing in-house programmes. Several reasons for the reticence of the pharmaceutical industry regarding outsourcing of lead optimisation can be identified.

First and foremost, the need for these services was simply not present. Until the late 1980s, the majority of the multi-disciplinary expertise required for lead optimisation could be found in major pharmaceutical companies (such expertise is widely recognised to be the result of extensive drug discovery project

experience). At that point in time, most major pharmaceutical companies considered that they had sufficient internal resources to advance their drug discovery programmes at an acceptable rate. However, the increasing pressure on the industry to be more productive, coupled with an increase in the number of 'druggable' targets emerging from genomics and proteomics approaches, encouraged pharmaceutical companies to undertake greater numbers of projects in the hope of generating the desired number of new chemical entities per year [5]. For major pharmaceutical companies, outsourcing represents an alternative to expensive infrastructure construction and hiring strategies. In the case of biotechnology companies, in the absence of major pharmaceutical companies in-licensing at the target or hit stage of the drug discovery process, many have sought proof-of-principle and added value by generating candidates against their biological targets. For many of these companies, the expense of building an internal lead optimisation department is too large; thus, outsourcing to a fast-moving, professional lead optimisation organisation has been required.

A second issue associated with outsourcing was that until the 1990s the external levels of expertise required to make outsourcing a viable alternative to internal effort were considered to be unavailable. The recent 'mega-mergers' and subsequent rationalisation of the internal research groups of major pharmaceutical companies have liberated a large number of scientists that are well-versed in lead optimisation to conduct their research in other guises. Many of these scientists have elected to pursue their careers in the biotechnology industry, but others have chosen to create customer-oriented, industry-proficient, fast-moving contract companies to meet outsourcing demands. For example, Argenta Discovery (<http://www.argentadiscovery.com>) has scientists of more than nine nationalities that have previously been employed by more than 20 different organisations. Furthermore, these scientists have experience of generating drug candidates and intellectual property (IP) in every known type of biological target and disease area.

The inherent conservatism of the pharmaceutical industry, which often lags behind other sectors in adopting new ways of thinking and working, is another obstacle to outsourcing by the major pharmaceutical companies [6]. The ultimate concern regarding outsourcing lead optimisation was, and still is, the security of information within such an outsourcing exercise. The data necessary to file composition-of-matter patents are typically generated during lead optimisation. These patents comprise the lifeblood of pharmaceutical companies and, therefore, must be protected implicitly. Perhaps it has taken time for companies to develop the level of trust required, or perhaps it has

been a simple matter of necessity – whatever the reason, this matter is now far less of an obstacle than it might have previously been, at least when outsourcing to the USA or European countries. However, some issues still remain with other countries.

Thus, over the past five years the outsourcing of lead optimisation has gradually become more commonplace. This has been something of a 'quiet revolution' in drug discovery, and has perhaps gone unnoticed amidst the much-hyped technologies that have been in vogue during the past decade.

Current players in the market

Brief profiles of more than 20 companies that are currently offering lead optimisation services are presented (note that companies that are dedicated to purely synthetic aspects of discovery chemistry, for example, fine chemicals and specialty chemicals, have been omitted. Several of these companies have been profiled recently [7,8]).

Albany Molecular Research

Founded in 1991, the resources of Albany Molecular Research (<http://www.albmolecular.com>) now include over 850 employees and facilities in New York, Chicago and Seattle. Consistent with its size, Albany Molecular Research offers a broad range of services including lead-seeking libraries (including natural products [9]), medicinal chemistry, combinatorial chemistry, computational chemistry, combinatorial biocatalysis, metabolism studies, chemical development, analytical services, physical chemistry, pilot plant and current good manufacturing practice (cGMP) synthesis [7,10]. The company is NASDAQ-listed as AMRI.

Argenta Discovery

Argenta Discovery was founded in 2000 by 25 ex-Aventis (<http://www.aventis.com>) scientists and ChemMediCa, which is a virtual spin-out company from Imperial College of Science, Technology and Medicine, UK (<http://www.ic.ac.uk>) [11–13]. The company now employs ~90 staff and is located in Harlow, UK. The company offers services spanning the breadth of lead optimisation activities including medicinal chemistry, parallel synthesis, microwave chemistry, assay development, biochemical screening, cellular screening, early ADMET (absorption, distribution, metabolism, excretion and toxicity) studies, analytical and physical chemistry and computer-aided drug design.

ArQule

ArQule (<http://www.arqule.com>) was founded in 1993 and currently employs ~300 staff at facilities in Woburn,

Medford and Norwood in the USA. The company initially specialised in high-quality library design and compound production but began moving to more of a drug discovery model in 1999, focusing on oncology targets. To this end, ArQule recently acquired Cyclis Pharmaceuticals, a company specialising in cancer biology [14]. ArQule first offered common stock to the public in 1996 and is listed on the NASDAQ as ARQL.

Array Biopharma

Founded in 1998, Array Biopharma (<http://www.arraybiopharma.com>) has its headquarters in Boulder, USA, where it employs 180 scientists [7,14]. The company offers a range of drug discovery capabilities including structural biology, high-throughput screening, informatics, lead generation, lead optimisation, analytical chemistry, drug metabolism studies and process R&D. The company is NASDAQ-listed as ARRY.

Asinex

Asinex (<http://www.asinex.com>) was founded in 1994 as a provider of compounds for screening but began offering chemistry services in 1998. The company now employs over 200 staff that are based in Moscow, Russia, and can provide services in computational chemistry, custom synthesis, library synthesis and biochemical screening.

Aurigene Discovery Technologies

Established in 2001, Aurigene Discovery Technologies (<http://www.aurigene.com>) is a Boston-based drug discovery organisation with research facilities in Bangalore, India [7,8,15]. Aurigene Discovery Technologies is a wholly owned subsidiary of Dr. Reddy's Laboratories (<http://www.drreddys.com>) and currently employs over 60 scientists. The company offers services in protein sciences, structure-based drug design, medicinal chemistry and natural product screening and synthesis.

BioFocus

BioFocus (<http://www.biofocus.com>) was founded in 1997 by former Wellcome (<http://www.wellcome.ac.uk>) scientists. The company initially focused on library design and synthesis, but this broadened following the acquisition of Cambridge Drug Discovery in 2001. BioFocus now employs 140 staff, with headquarters and research facilities in Cambridge, UK [13,16,17]. The services offered by BioFocus comprise assay development, biochemical screening, hit-to-lead and lead optimisation, informatics, library design and synthesis and ADMET property prediction. The company is quoted on the Alternative Investment Market (AIM) of the London Stock Exchange.

Chembiotek Research International

Chembiotek Research International (<http://www.chembiotek.com>) was founded in 2000 by the Chatterjee Group. The company is based in Kolkata, India, and currently numbers over 70 employees. Services offered include synthetic and/or process research, computational chemistry and biology, combinatorial chemistry, lead optimisation and natural product synthesis.

ChemBridge Research Laboratories

ChemBridge Research Laboratories (<http://chembridge-research.com>) was founded in 2000 as a spin-off of ChemBridge Corporation (<http://chembridge.com>), an established provider of screening compounds and building blocks [17]. The company is based in San Diego, USA, and offers targeted and custom libraries together with medicinal chemistry and ADME services.

Chemical Diversity Laboratories

Founded in 2000 as a wholly owned subsidiary of ChemDiv (<http://www.chemdiv.com>), Chemical Diversity Laboratories now employs more than 200 chemists based in San Diego and Moscow [7,18]. The company specialises in target-directed libraries, hit-to-lead and lead optimisation services, computational chemistry and biochemical screening.

ChemOvation

Formed in 1999 with backing from the Novartis Venture Fund (<http://www.venturefund.novartis.com>), ChemOvation (<http://www.chemovation.com>) was acquired by KuDOS Pharmaceuticals (<http://www.kudospharma.co.uk>) in 2000 [17,19]. ChemOvation employs ~35 people and is based in Horsham, UK. The company offers services in organic chemistry, medicinal chemistry, analysis and purification, computational chemistry, biochemical screening, ADME and toxicology, early process development and scale-up.

Comgenex

Comgenex (<http://www.comgenex.com>) was founded 1992 and is based in Budapest, Hungary. The company provides a range of services including chemogenomics, protein expression, assay development and screening, library synthesis, medicinal chemistry, ADMET services and chemoinformatics.

deCODE genetics

deCODE genetics (<http://www.decode.com>) acquired MediChem Life Sciences in 2002 [7]. The company continues to offer contract services, in addition to applying the ex-MediChem capabilities (based in Woodford, USA, and

Bainbridge Island, USA) to its own research programmes. The contract services offered include structural biology, lead discovery and optimisation, ADME profiling and cGMP scale-up.

Discovery Partners International

Founded in 1998, Discovery Partners International (<http://www.discoverypartners.com>) now has ~240 employees and is headquartered in San Diego with operations in the USA, Europe and India [7,13]. Services offered by the company include target characterisation, targeted and screening library design and synthesis, high-throughput and high-content screening, lead generation and optimisation, gene expression analysis and protein crystallisation. Discovery Partners is NASDAQ-listed as DPII.

Evotec OAI

Evotec OAI (<http://www.evotecoi.com>) was formed in 2000 from the merger of Evotec BioSystems AG and Oxford Asymmetry International (OAI) [7]. The company currently employs over 600 people in Hamburg, Germany, and Abingdon, UK, and offers services in assay development and screening, compound library synthesis, lead optimisation, ADMET profiling, process R&D, scale-up and manufacture. Evotec OAI is listed on the Deutsche Börse as EVT.

GVK BIOSCIENCES

Founded in 1999, GVK BIOSCIENCES (<http://www.gvkbio.com>) now has more than 60 staff. The company is based in Boston, USA, with research facilities in Hyderabad, India. Current services offered include informatics, medicinal chemistry and clinical R&D [7,8]. In 2002, a three-year deal was signed under which Ricerca Biosciences (<http://www.ricerca.com>) became the exclusive worldwide partner for access to the medicinal chemistry services provided by GVK BIOSCIENCES [10].

Kalexsyn

The newest company to appear on the outsourcing scene is Kalexsyn (<http://www.kalexsyn.com>), which was founded in 2003 by former Pfizer (<http://www.pfizer.com>) medicinal chemists [20]. The company offers expertise in structure-activity relationship (SAR) development, lead optimisation, ADMET problem solving, synthetic organic chemistry, asymmetric synthetic techniques, heterocyclic chemistry and parallel-synthesis techniques.

NCE discovery

NCE discovery (<http://www.ncediscovery.com>) was started in 2001 as a spin-out company from the Wolfson Institute for Biomedical Research, UK (<http://www.ucl.ac.uk/WIBR>),

and has recently opened new headquarters and laboratories on the Cambridge Science Park. The company provides services in hit-to-lead and lead optimisation, lead development, molecular modelling and related consultancy.

NiKem Research

Formed in 2001 as a spin-out from GlaxoSmithKline, Italy (<http://www.gsk.com/index.htm>), NiKem Research (<http://www.nikemresearch.com>) undertakes contract work in lead finding, hit validation, lead optimisation, ADMET profiling and combinatorial chemistry.

Peakdale

Since its creation in 1992, Peakdale (<http://www.peakdale.co.uk>) has grown to employ more than 65 staff that are based in Chapel-en-le-Frith, UK [7,9,10,12,21,22]. Services offered include hit discovery, patent exemplification, lead optimisation, custom synthesis and parallel synthesis.

Pharmacopeia

Pharmacopeia (<http://www.pharmacopeia.com>) was formed in 1993. Today the company comprises drug discovery services and a software division (Accelrys; <http://www.accelrys.com>). However, there are plans to spin-off Pharmacopeia Drug Discovery as a separate entity [23]. The combined operation employs ~800 people and has its headquarters in Princeton, USA. In 2003, Pharmacopeia announced the formation of a strategic partnership with WuXi PharmaTech (<http://www.pharmatechs.com>) to provide contract chemistry services and research development to pharmaceutical and biotech companies worldwide at highly competitive prices [17]. Among the services offered by Pharmacopeia are combinatorial chemistry, medicinal chemistry, high- and ultra high-throughput screening, *in vitro* pharmacology, molecular modelling and informatics. Pharmacopeia is NASDAQ-listed as ACCL.

Ricerca Biosciences

Founded in 1961, Ricerca Biosciences has been privately owned by SG Capital Partners (<http://www.sgcapiatpartners.com>) and Venture Biologics since 2000. The company has 225 employees and is located in Cleveland, USA. Among the services offered by Ricerca Biosciences are medicinal chemistry, *in vitro* ADME screening, metabolism studies, *in vivo* toxicology, *in vivo* pharmacology, process chemistry, pilot plant work and analytical chemistry. Ricerca Biosciences has an exclusive partnership with GVK BIOSCIENCES whereby Ricerca Biosciences can access up to 100 India-based medicinal chemists [10].

Scynexis™

Scynexis™ (<http://www.scynexis.com>) was founded in 2000 by former Aventis scientists. The company now employs ~125 staff at locations in Research Triangle Park, USA, and Ongar, UK [24,25]. Services offered include combinatorial chemistry, medicinal chemistry, early ADMET studies, analytical chemistry, radiochemistry, custom synthesis and process chemistry.

Tripes

In 1997, Tripes (<http://www.tripes.com>) acquired Receptor Research, a spin-off from Maybridge (<http://www.maybridge.com>). Tripes Receptor Research now employs more than 80 scientific staff that are located in the UK [10,11]. The company provides services in hit-finding, hit-validation and lead optimisation. Tripes is NASDAQ-listed as TRPS.

WuXi PharmaTech

WuXi PharmaTech was established in 2001 by Ge Li (also a founder member of Pharmacopeia). The company presently employs ~190 scientists that are based in Shanghai, China [7,26]. Services offered by WuXi PharmaTech include library design and synthesis, medicinal chemistry and lead optimisation, radiochemistry, manufacture of pharmaceutical raw materials and *in vivo* pharmacokinetic studies.

Current trends in the market

Several trends can be identified in the lead optimisation outsourcing market. Table 1 collates some of the recent deals made by the companies profiled. The table supports one of the findings of a recent market research report [2]: the majority of major pharmaceutical companies are now availing themselves of outsourced lead optimisation services [27]. There are few names among the major pharmaceutical companies that are absent and the table only presents selected deals that have been announced in 2003–2004 at this point in time – there are almost certainly other deals that have not been disclosed. The companies engaging outsourcing services are from all the major pharmaceutical markets – the USA, Europe and Japan. It is a truly global phenomenon.

Several companies have moved into the lead optimisation services market to take advantage of the new opportunities it presents. Some companies that once specialised in supplying compounds for high-throughput screening and reagents for synthesis have broadened their offerings to include medicinal chemistry and allied services. Good examples of this trend are companies such as ChemDiv, ChemBridge and Asinex. Several companies that initially produced combinatorial libraries for sale have also

metamorphosed into more-rounded entities with broader capabilities. Some have gained new proficiencies through acquisition (e.g. BioFocus) and others through mergers (e.g. Evotec OAI). As a result, the marketplace for high-value integrated drug discovery services is becoming increasingly competitive.

Perhaps in response to increasing competition, some of the more-established companies have been moving away from a purely service-based business model by also carrying out proprietary drug discovery research. A good example of a company following this trend is ArQule, which is increasingly focusing on oncology-based drug discovery [14]. Another example is Array Biopharma, which has recently formed a deal with AstraZeneca (<http://www.astrazeneca.com>) for one of its in-house kinase inhibitor programmes. Argenta Discovery has always been based on this kind of model, realising that although contract services can be a source of revenue, it is IP that really drives the valuation of a company in a positive direction. Argenta Discovery is currently looking to out-license a histone deacetylase inhibitor project, thus making the definition of ‘outsourcing lead optimisation’ an even broader one.

The move towards ‘off-shoring’, outsourcing to countries such as India, China and the former Soviet Union, is a burgeoning phenomenon [7,8,26]. This explains the inclusion of companies such as WuXi PharmaTech, Aurigene Discovery and GVK BIOSCIENCES in the list of companies profiled. In 2004, it is expected that over US\$200 million worth of pharmaceutical- and biotechnology-related work will be outsourced to India [28]. China is the focus of growing interest from major pharmaceutical companies. Early indications of this include the deal formed between WuXi PharmaTech and Merck (<http://www.merck.com>) [26] and the collaboration between Shanghai ChemExplorer and Eli Lilly (<http://www.lilly.com>) for chemical synthesis and compound selection projects [29]. Companies based in countries such as China and India are able to offer extremely competitive full-time equivalent (FTE) rates compared with their US and European counterparts (e.g. labour costs in India are typically 50–90% lower than in the Western world [30]), as well as the services of highly educated and experienced staff, some of whom have trained or studied abroad before returning to their homelands. At the present time, it is probably the case that most of the work outsourced to these countries is primarily organic synthesis, for example, the provision of custom reagents, or specific compounds, rather than medicinal chemistry. This is mainly because of continuing concerns over the security of IP in these countries [31]. However, on 1 January 2005, India will adopt a patent regime that conforms to the

Table 1. Recent deals announced by companies providing lead optimisation services

Company providing lead optimisation service	Outsourcing company	Current selected deals announced in 2003–2004
Albany Molecular Research	Eli Lilly Affinium Pharmaceuticals	Natural products research collaboration Strategic research alliance in anti-infectives
Argenta Discovery	Corcept Therapeutics Teijin Aventis GSK AstraZeneca	Discovery and optimisation of second-generation drug candidate for a psychiatric disorder Lead optimisation against cardiovascular target 'Umbrella agreement' for a wide range of services Provision of discovery research capabilities to two of GSK's Centres for Excellence in Drug Discovery Provision of discovery research capabilities
ArQule	Novartis Institute for Biomedical Research	Generation and optimisation of small-molecule compounds for anti-infective drug discovery programme
Array Biopharma	GenPath Replidyne AstraZeneca Genentech	Collaboration to identify small molecules that target a novel tumour maintenance gene Collaboration to generate small molecules targeting bacterial infections Licensing and collaboration agreement to develop Array Biopharma's MAP-ERK programme in the field of oncology Licensing and collaboration agreement for multiple targets in the field of oncology
Asinex	Ribotargets Avalon Pharmaceuticals Biovitrum Janssen Pharmaceutica F2G Asahi Kasei	Exclusive compound access deal Lead optimisation of screening hits (recently extended by one year) Late-stage lead optimisation Extension of discovery chemistry agreement signed in 2002 Drug discovery collaboration Optimisation of hit compound
BioFocus	Amgen Mitsubishi Roche Ferring AstraZeneca	Ion channel-based drug discovery collaboration High-throughput screening services Design and supply of kinase-directed compound libraries Discovery of novel lead compounds Access to BioFocus' thematic analysis technology
Chembiotek Research International	Angenix	SAR studies on lead compounds
ChemBridge Research Laboratories	Tanabe Memorial Sloan-Kettering Cancer Center GSK Pfizer	Synthesis of focused compound libraries and support of drug discovery programmes Compound supply agreement for anticancer drug discovery Deal to access the GPCR-targeted library of ChemBridge Research Laboratories Expansion of existing agreement to include support of discovery chemistry

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Table 1. Recent deals announced by companies providing lead optimisation services (continued)

Company providing lead optimisation service	Outsourcing company	Current selected deals announced in 2003–2004
Chemical Diversity Laboratories	Mpex Pharmaceuticals	Supply of compounds and chemistry services
	Biogen	Supply of synthetically feasible compounds for virtual screening
	Sienabiotech	Supply of aspartyl protease-directed compound library
	ESBATEch	Supply of maximally diverse library for screening
ChemOvation	Cancer Research Technology	Computational and medicinal chemistry services
	Avidex	Medicinal and synthetic chemistry services
	Trophos	Provision of medicinal chemistry and synthetic chemistry services
Comgenex	Bayer Healthcare	Provision of exclusive compound libraries
deCode genetics	Families of Spinal Muscular Atrophy	Lead optimisation and scale-up
Discovery Partners International	Novartis	Assay development and biological screening
	Actelion	Collaborative agreement for access to drug discovery capabilities
	Seikagaku Corporation	Assay development and biological screening
	Kyorin Pharmaceutical	Assay development and hit identification
	Inspire Pharmaceuticals	Lead optimisation of compounds active against the P2Y receptor family
	Allergan	Lead finding collaboration for GPCR and enzyme targets
	Celltech	Drug discovery collaboration aimed at intracellular signal transduction target
Evotec OAI	Pfizer	Expansion of ongoing compound provision agreement
	Oxagen	Hit-finding services
	Psychiatric Genomics	Design of focused libraries and ADMET profiling
	Dynogen Pharmaceuticals	Hit-candidate services
	Novartis	Assay development and screening
	Artesian Therapeutics	Optimisation of small-molecule therapeutics for congestive heart failure
	Axxima Pharmaceuticals	Lead optimisation of kinase inhibitors
	Roche	Identification and optimisation of anticancer compounds
	Rib-X Pharmaceuticals	Medicinal chemistry partnership to identify novel antibiotics for clinical development
	Toray Chemical Industries	Integrated medicinal chemistry, virtual screening and compound profiling agreement
NCE Discovery	Inploid	Hit-to-lead work on novel anticancer agent
	Trigen	Optimisation of small molecule cardiovascular drug candidate
	BiolImage	Compound selection for screening

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Table 1. Recent deals announced by companies providing lead optimisation services (continued)

Company providing lead optimisation service	Outsourcing company	Current selected deals announced in 2003–2004
NiKem Research	Wyeth	Compound synthesis agreement
	GSK	Provision of focused combinatorial libraries and medicinal chemistry support; research and development agreement for the discovery of ORL-1 modulators
	Newron Pharmaceuticals	Optimisation of leads against CNS targets
	Chiesi Farmaceutici	Collaboration on a discovery programme in respiratory disease
Peakdale Molecular	Pfizer	Compound synthesis agreement
	GSK	Provision of dedicated team of chemists to work with GSK's Respiratory and Inflammation Centre of Excellence for Drug Discovery
Pharmacopeia	Celgene	Lead identification
	Novartis	Lead identification
	AstraZeneca	Lead identification
	Schering Plough	Lead identification and optimisation
	Neurocrine Biosciences	Lead identification
	Altana	Identification and optimisation of small-molecule lead compounds for advanced development
	Taiho	Identification of promising small-molecule lead compounds suitable for further development
Ricerca Biosciences	The Cleveland Clinic	Collaboration on initial development and testing of a cancer-killing agent
Scynexis	Molecular Engines Laboratories	Discovery and development of anticancer therapeutics
	Merck	Discovery and development of anti-infectives
	Roche	Discovery and development of compounds for metabolic and CNS disorders
	GeneCare Research Institute	Drug discovery, synthesis and purification services
	Mitsubishi Pharma	Development of high-purity compound libraries for screening
Tripos	Critical Therapeutics	Identification and optimisation of agonists for a nicotinic acetylcholine receptor
	Biovitrum	Design and synthesis of lead compounds
	Chronogen	Three-year collaboration to discover and optimise small-molecule therapeutics for cardiovascular disorders
	Pfizer	Amendment to ongoing strategic collaboration for the design, synthesis and purification of drug-like compounds
WuXi PharmaTech	Pharmacopeia	Strategic alliance to provide contract chemistry services at highly competitive prices
	Merck	Multi-year research collaboration including creation of new drug discovery libraries and constituents to advance lead optimisation programmes

Abbreviations: ADMET, absorption, distribution, metabolism, excretion and toxicity; CNS, central nervous system; GPCR, G-protein-coupled receptor; GSK, GlaxoSmithKline; MAP-ERK, mitogen-activated protein kinase–extracellular-signal-related kinase; ORL-1, Opioid Receptor Like-1; SAR, structure–activity relationship.

Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement as a corollary of its membership of the World Trade Organisation (WTO) [32]. China joined the WTO in 2001 and should therefore be expected to follow suit in the future. Once these safeguards are in place, there could be less reluctance to outsource the more sensitive, IP-generating tasks to these countries.

Some US outsourcing companies have been quick to seize on the opportunities offered by off-shoring. The liaisons between Pharmacopeia and WuXi PharmaTech [7] and Ricerca Biosciences and GVK BIOSCIENCES [10] intend to offer clients the best of both worlds – the security and industrial experience of the West and the cost-efficiency of the East. Discovery Partners International has also set up a small operation in India creating combinatorial and focused libraries [7]. This is a trend that seems likely to continue.

Conclusion

In such a fast-moving market, it is hard to see clearly where the future lies. The increase in the level of lead optimisation outsourced by pharmaceutical companies is projected to continue, although there will doubtless be ebbs and flows that are driven by other factors that impinge upon the pharmaceutical industry. It could be that competition from off-shoring will drive some of the smaller US and European companies out of business, or at least force consolidation in the market. Others might adopt a business model that embraces off-shoring, as some of the US companies seem to be doing. Alternatively, some companies might change direction completely and move from service provision to become drug discovery companies concentrating on the sale of potential drug candidates for development. Whatever happens, it seems certain that in the wake of the quiet revolution, constant change is here to stay.

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