

SHARING RISKS AND REWARDS

basis for a turnkey pharma-biotech alliance in osteoarthritis

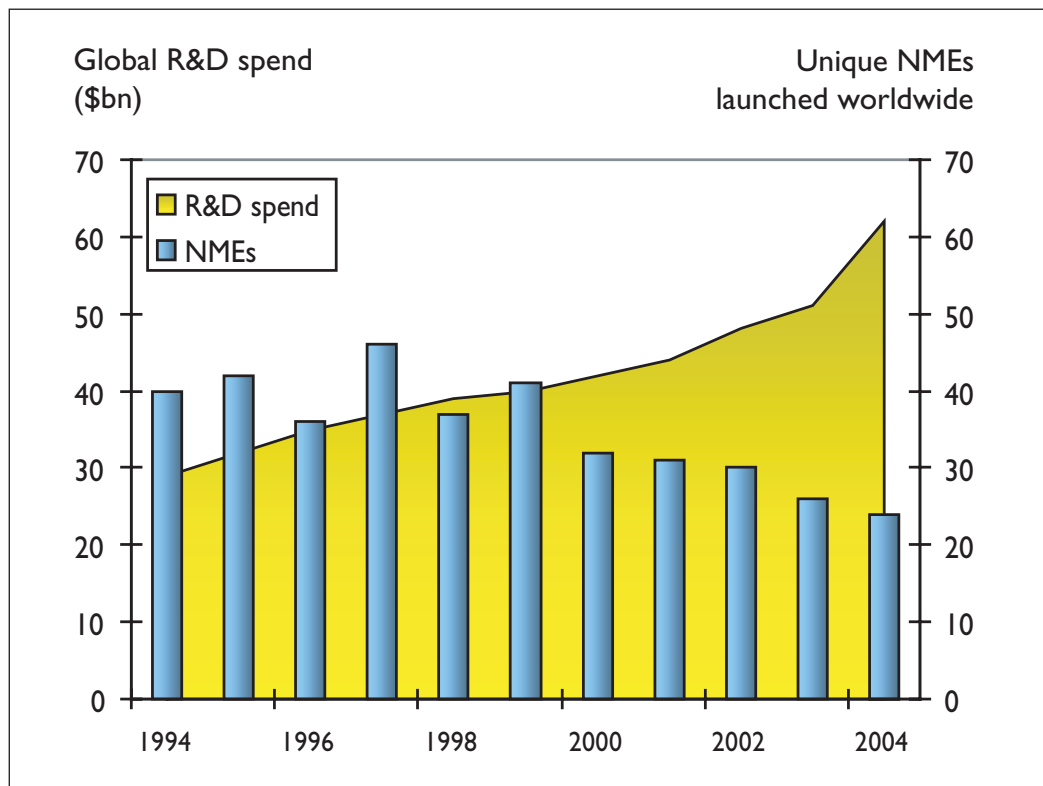
In June 2006, Galapagos and GlaxoSmithKline's Center of Excellence for External Drug Discovery (CEEDD) formed a multi-year worldwide alliance to discover and develop novel drugs for osteoarthritis. The focus of the alliance will be on delivering disease-modifying drugs with clinical Proof of Concept for osteoarthritis to GSK's global R&D organisation. The alliance capitalises on the synergies of Galapagos' innovation in drug discovery and GSK's understanding of the disease as well as its track record in moving compounds from clinical Proof of Concept to commercialisation. This review describes the roles for each party in the alliance and analyses the reward-risk sharing model that forms the basis of this pharma-biotech alliance.

It is evident that the pharmaceutical industry as a whole is going through a challenging time, a time that calls for change and transition. For many years, blockbuster drugs have carried the pharma industry with record revenues and profits. Over the past decade, the industry has witnessed a decline in the number of launches of new medicines each year. As a consequence, the pharmaceutical companies face a product pipeline gap that cannot be closed by current in-

house drug development efforts. In addition, expiration of patents on a large number of blockbuster drugs puts pressure on the industry to fill pipelines with innovative new drugs. Simultaneously, global expenditures for research and development have continued to increase. It is estimated¹ that global R&D investments have risen 70% since 1995, while output of new molecular entities has fallen by 40%, as illustrated in **Figure 1**.

Dr Andre Hoekema

Figure 1
Industry troubles (1994-2004)¹



Evidently, R&D productivity in the pharma industry is slowing down, despite significant increases in funding. Because of this lack of progress, the pressure for change is on and pharmaceutical companies are indeed looking for ways to turn the tide. Two clear trends observed throughout the industry are i) pharma’s focus on the level of R&D spending, and ii) improving timelines to develop and market

opportunities to expand their product development pipeline through M&As, in-licensing of clinical drug candidates as well as through alliances with biotechnology companies in selected disease programmes.

Establishing alliances to secure innovation has become critical for pharma to fill their product pipelines. Therefore, pharma companies have increasingly started to outsource portions of their drug discovery efforts to biotech.

For biotech companies, such alliances can serve to balance the increasing costs for drug discovery and development, thus maximising returns from their research.

With both pharma and biotech companies having incentives to pursue alliances, it should come as no surprise that deal making is accelerating rapidly. Over the last five years, more than 700 collaborative agreements were signed between pharma and biotech companies. This paper reviews one such alliance: the osteoarthritis alliance between Galapagos and the GSK CEEDD.

Disease background

Osteoarthritis (OA) is the most common form of arthritis, characterised by joint destruction and loss of cartilage – causing pain, swelling and loss of motion of the joint. Because there are no

“We’ve got 20,000 scientists fishing for ideas in our lake – if there’s a fish, then we’re going to catch it. The trick is now to go out and cast the line in other people’s lakes to find their exciting scientific programmes.”
Jean-Pierre Garnier, CEO GlaxoSmithKline

new drugs. As a result, pharma companies are focusing on their core competencies: late development, registration and sales and marketing of drugs. Furthermore, they are aiming to improve flexibility, limit overhead and gain access to novel technologies and products. Indeed, pharmaceutical companies are looking for more

therapies available that prevent or block the progression of osteoarthritis, the potential unmet need is substantial.

It is expected that with the ageing of the population, more individuals will be prone to develop OA. As mobility of seniors is of high importance to maintaining a high quality of life, preventing the severity of OA is seen as an immense clinical need over the next decade.

The search for OA disease modifying drugs

Most currently marketed drugs were discovered through a traditional drug discovery process that involved screening compounds in disease models. Understanding the intracellular processes that underly the disease is important to increasing the success of drug screening.

With this in mind, Galapagos built a target discovery and validation platform based on assaying gene function in human primary cells. The company has focused collections of arrayed recombinant adenoviruses harbouring the drugable genome, for either knock-down or knock-in of individual pro-

teins in cellular disease models. These collections have a proven track record in disease biology driven identification and validation of novel drug targets in a range of indications.

For drug discovery in OA, Galapagos identified novel targets that stimulate anabolic repair processes for early stage OA (chondrogenesis) and inhibit catabolic (breakdown) activity in affected joints for late stage OA, using human primary articular chondrocytes (HACs), the main cell types in cartilage.

Galapagos developed cellular assays to measure chondrocyte differentiation and maintenance. Galapagos' adenoviral libraries containing the drugable genome were screened in these assays to identify drugable targets that regulate chondrocyte differentiation and normal function. These hits were then validated through a selection of secondary validation assays, and formed the basis for high throughput compound screening. Treatment with the novel compounds results in an effective increase in cartilage in an animal model, indicating their potential effect to revert the disease in osteoarthritis patients.

Risk sharing in drug discovery

The drug discovery process can be divided into several phases, starting from the search for drug targets through to launching and marketing a novel medicine. **Figure 3** shows an overview of these phases, including the main activities and estimates of each phase's duration, based on historical statistics. Each phase has its own profile in terms of requirements for technology and expertise, as well in terms of risk, duration and funding needs.

Alliance structure and purpose

Galapagos' role in the alliance is to execute the early discovery and development phases of this process. This includes expanding the OA target portfolio, conducting compound screening on these targets, identifying tractable chemical hits, pursuing hit-to-lead programmes, and developing resulting leads into candidate selection compounds through to a successful Proof of Principle and Proof of Concept in clinical research Phase IIA. GSK would have the option to take over responsibility for developing the compound when it has achieved the agreed criteria for candidate selection, Proof of Principle or Proof of Concept. GSK will be responsible for executing all development activities for the compound following the exercise of its option and GSK will have an exclusive right to commercialise these compounds worldwide.

Galapagos will have the right to further develop and commercialise compounds for which GSK does not exercise its option.

Companies of all types sign collaborative agreements with the aim to build value, extend product pipelines, reduce costs, or fill gaps in capabilities. The primary driver for alliances is generally the notion that a combination of complementary resources and capabilities can create value. Alliances also allow its participants to reduce risks, whether technological, market-related or competitive, by sharing it. The essential element that defines the structure of this deal is the sharing of risks as well as rewards between Galapagos and GSK.

For GSK, this risk-sharing principle provided a clear driver for success in enhancing the late stage product portfolio and increases R&D capacity without increasing fixed costs.

For Galapagos, the alliance provides access to significant funds in both the near and long term to support its ongoing R&D. Moreover, both parties will be able to benefit once success is reached. As such, the alliance shares the risk of developing OA therapies.

Each party brought capabilities to the alliance that the other party valued; Galapagos was looking for a collaborator with vast experience in late stage clinical development, registration and

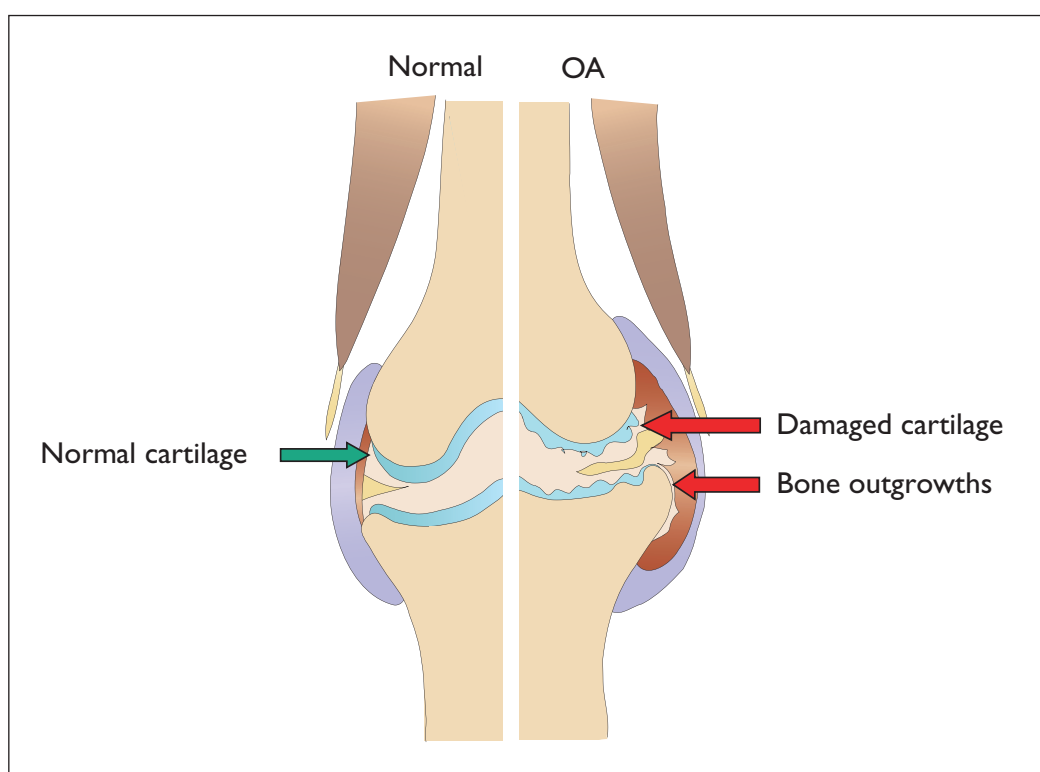
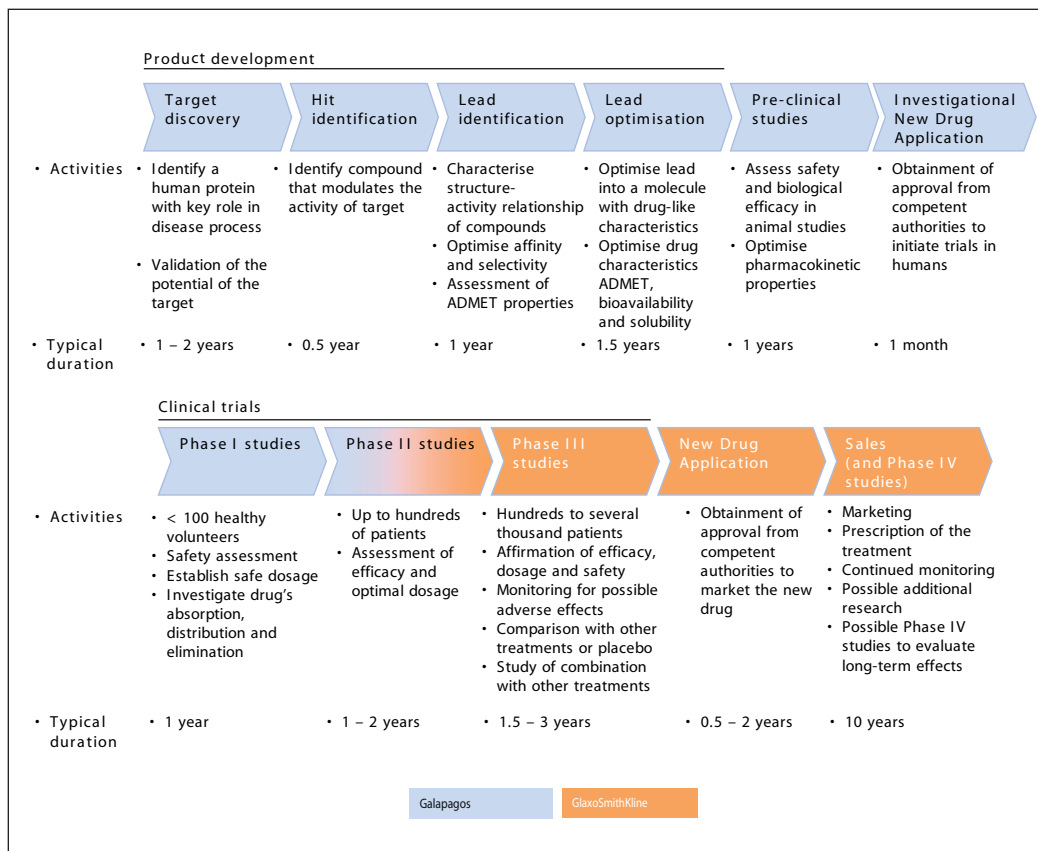


Figure 2
Joints affected and unaffected by OA

Figure 3
Overview of the drug discovery process and roles of partners



References

I CMR Pharmaceutical Factbook, September 2005.

commercialisation. GSK needed a collaborator that would bring an innovative approach and expertise in early drug discovery.

In structuring the deal, the parties were able to define a milestone-based funding structure that met both parties' objectives. The milestones cover a variety of pre-defined events from the generation of novel target sets to regulatory approval of an OA therapeutic compound.

Summary of the alliance

- Exclusive for osteoarthritis.
 - Galapagos to deliver molecules with clinical PoC (phase 2a) to GSK drug development.
 - Gene to clinical Proof of Concept for multiple targets in osteoarthritis.
 - Up to €137 million in milestones for two marketable products.
 - Up to double digit royalties on commercial sales of alliance products.
- DDW**

Director of Corporate Development Europe. He brings 20 years of biotech experience from positions at Molecular Probes Europe (Managing Director), Crucell (Director of Business Development), DSM Life Sciences and MOGEN (Research and Project Management) and Genentech, Inc (R&D). Dr Hoekema has a PhD degree from Leiden University and is the inventor of more than 20 series of patent applications, resulting in 15 patents issued in the US.

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