The Strategic Contributions of Indian Operations in AMRI's Global Outsourcing Organization

WHITE PAPER

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The concept of outsourcing, though late in adoption by pharmaceutical research and development organizations relative to other industries, has gained strong acceptance over the past 15 years, and Contract Research Organizations (CROs) have been established to meet most of the needs of the research industry. Furthermore, within the past decade, factors pointed to by Thomas Friedman in his 'flattening' of the earth thesis, coupled with the return to India and China of highly educated and trained industrial scientists, and the institution of stronger controls on the treatment of intellectual property in these countries have led to the creation and rapid growth of a competitive sector of low cost, contract services organizations that have experienced rapid acceptance and today successfully compete with Western-based CROs.

As long time partners in the industry, CROs have been greatly affected by dynamic changes in the universe of available customers and in the competitive landscape. Many CROs have come and gone in the feast or famine relationships that have followed the multiple boom/bust cycles in the industry; and those remaining continue to be squeezed in a globally competitive environment. In spite of recent budget trimming in the research industry and fewer pharma and biotech companies remaining, it is actually now assumed that the use of CROs will broaden and grow. To be an effective partner, CROs need to continue investing in facilities, people, equipment, services and technologies in order to meet the increasing needs of an evolving industry.

Today it is widely accepted that most, if not all, functions in drug discovery and development can be outsourced. Although CROs tend to specialize around core technologies, functions and even geography, the lines separating these specializations continue to blur. In small molecule drug discovery and development, outsourcing continues to evolve from tactical services to more strategic relationships. Functions outsourced include, but are not limited to, high throughput screening, library synthesis, custom synthesis, medicinal chemistry SAR synthesis, small scale process development, *in vitro* and *in vivo* biology efficacy testing, *in vitro* and *in vivo* ADME, formulation development or manufacturing, analytical development and testing, GMP synthesis of intermediates or API, bioanalytical testing and fermentation. More and more outsourcing is focusing on strategic and customized applications of several of these functions bundled together in order to take advantage of organizational synergies, decrease timelines and, more importantly, to yield greater value per outsourcing dollar.

Because of, or in spite of these trends, however, the definition of value remains ill defined industry wide. To procurement groups, which have been yielded greater decision making authority in most large multi-nationals, value and price are often deemed synonymous; to the detriment of their employers. To scientific research leaders, value is better defined as successful outcomes (new drugs in the clinic or, better, new drugs on the market) per dollar spent, but the correlation of this metric to research activity is just as difficult to quantitate today among outsourcing providers as it has ever been to judge internally. The obvious conclusion is that true value is some combination of the two, and as the better low cost providers gain experience and training, their ability to contribute greater value will only improve over time. The challenge for the drug industry and its long term objectives, though, is to ensure that in pursuit of lowering overall costs, CRO providers are able to make a reasonable return such that they can continue to invest in ways that ultimately benefit their ability to offer greater value for their customers.

As one of the first outsourcing CROs to focus on chemistry services, Albany Molecular Research, Inc. (AMRI) was founded in 1991 in New York, on the belief that the industry was resource limited in its capacity to discover and develop new medicines. By the latter 1990's, and in concert with the beginning acceptance of the industry to outsourcing, AMRI grew rapidly and continued to expand its service offerings to eventually encompass *in vitro* biology and multiple facets of small molecule drug discovery research, development and cGMP API manufacturing. The period around the millennium was robust, both for the pharmaceutical and biotechnology industries, and also for companies like AMRI, who supported the research industry as a high quality outsourcing provider. It was also a golden time for research employment, as research budgets grew significantly, and companies desperate for employees, embraced the H1 visa as a tool to employ foreign born, western educated scientists. The main catalysts that changed multiple industry dynamics were the collapse of the stock market bubble in 2000 and the terrorist attacks on New York and Washington on September 11, 2001.

Having accepted outsourcing as a means to leverage internal resources and expand the number of programs that could be researched and developed, the significant growth of R&D budgets among large pharmaceutical companies came under pressure. Variable spending moved under the microscope and outsourcing was one of the few areas that could be cut while preserving internal headcount. At the same time, these companies had accepted outsourcing as a strategic vehicle to leverage internal resources, and with the emergence of low cost providers primarily in India and China, a few companies began to experiment and put selected projects into these countries.

The period between 2002 and 2004 was one of great change for companies like AMRI. As pressures increased on research-based companies to evaluate R&D spending, more and more outsourcing decisions were driven by pricing over all other factors. An added impetus to expand or spend in China or India was the opportunity to gain strategic access to the markets in these large countries, which promise to continue evolving and grow in size and importance.

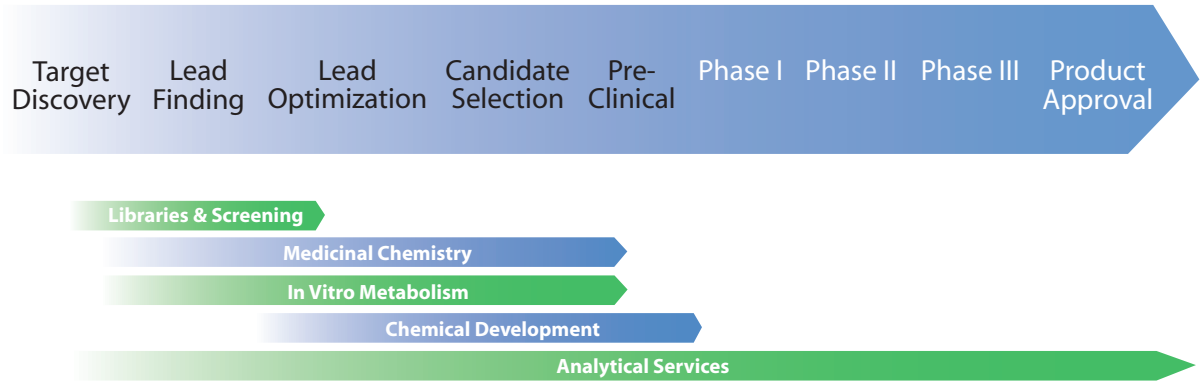
The drug industry has a history over the last couple of decades of following the latest fad, only to abandon it as the glamour fades and move on to the next one. In AMRI's view, the major shift of outsourcing to Asia and other lower cost structure countries was a trend, not a fad, and we felt a need to adapt our organization to the new reality if we wanted to return to the rapid growth we had experienced in the late 90's. The initial test projects of industry outsourcing with low cost structure vendors morphed into sizable deals, as nearly every large pharma company in the U.S. established and grew significant relationships beyond its borders.

Having perceived this trend as real and long term, AMRI made a commitment in 2003 to become a global organization. A task force was formed to evaluate international locations that might complement AMRI's US-based operations. Criteria that were evaluated included (to name a few): the presence of an educated and qualified workforce, country experience in pharmaceutical research, development or manufacturing, a competitive cost structure relative to the West, communication capabilities, and political stability. Another criteria was proximity to untapped markets, which would allow AMRI to compete for business from companies in countries we had not historically worked with. Strategically, this last criteria was as important as the others as AMRI sought to become a global organization, not only in location but in customer base.

After evaluating multiple country locations, AMRI selected India and Singapore for its initial offshore investments. In 2004, AMRI officially became global by opening laboratories in Singapore, which initially were focused on small molecule drug discovery chemical synthesis. Several months later, AMRI opened laboratories in Hyderabad, India. Here the focus was on custom synthesis, medicinal chemistry support, chemical development and kilo lab scale chemical synthesis. Both Singapore and India were greenfield investments, not acquisitions. Later, AMRI acquired labs in Budapest, Hungary (now named AMRI Hungary) from ComGenex, a company that initially was formed to provide custom and off the shelf chemical libraries. Most recently, AMRI's February, 2010 acquisition of Excelsyn (now AMRI UK) in Holywell, Wales, affords additional process development, pilot plant and API manufacturing services. These facilities each met the criteria established above and put the company in closer proximity to potential new customers in Europe and around the world.

Over time, AMRI has continued to invest in expansion of all of its international and domestic locations, adding capabilities, equipment, key personnel and additional space. AMRI's India presence evolved with the acquisition of multiple non-GMP intermediate and GMP manufacturing facilities in Aurangabad, as well as the construction of a new laboratory building in Hyderabad. A further expansion in Hyderabad is currently underway. Similarly, AMRI Singapore has experienced similar growth to Hyderabad, relocated to new laboratory space and also opened new laboratories that provide *in vitro* biology services, either alone or in support of integrated medicinal chemistry projects.

Spectrum of Capabilities in Asia



It is beyond the scope of this article to include a discussion of the added challenges of managing multiple sites with overlapping capabilities and cost structures. Suffice it to say, in spite of these challenges, the synergies are readily apparent. From the beginning, AMRI's strategy was to offer a blended model in which scientists or other personnel at multiple locations could be assigned to any given project. Under such a hybrid or integrated business model, projects can be resourced at multiple sites in different regions of the globe, thereby offering regional expertise, ensuring western quality and performance standards are maintained, and providing the benefit of a blended cost structure, all factors in maximizing value to the customer. Such projects could be built around discovery services, as well as chemical and analytical development and intermediate and GMP API manufacturing. A direct and immediate benefit to the customer is the removal of a need to man their outsourced projects to low cost providers with their own resources, in order to train the provider's staff, project manage the program, and help or even lead decisions in solving problems that crop up in the ordinary performance of scientific research.

In integrating projects performed at two or more of our global locations, AMRI created a Global Project Management operations function, which is responsible for representing the customer's interests, deal with logistical issues that may occur, and be a single point of contact. The Global Project Management (GPM) team is comprised of a flexible group of individuals with significant industry experience. Staffed by a leader located at one of our US sites, as well as containing members located at each of the facilities, the team's responsibility is to minimize communication issues, and better leverage AMRI's capabilities to current project needs, ensuring appropriate problem solving and performance capabilities are being applied.

Regardless of where the project may be staffed, the team has access to the extensive literature and search capabilities of our US locations, and can tap into the collective problem solving and brainpower of industry experienced managers as needed. The result of AMRI's globalization and Integrated Business Model is the ability to offer a competitive, best in class outsourcing option for the industry.

Numerous projects are in progress or have been completed using this hybrid, integrated model at AMRI. AMRI's operations in Hyderabad and Aurangabad, India are especially well suited to be a centerpiece of a global, integrated project team, as highlighted in the case studies that follow.

Case Study 1.
A fee for service program was undertaken to conduct two hit-to-lead optimization programs for a metabolic disorder target. Chemistry was initiated at AMRI's Hyderabad laboratories with multiple full-time equivalents (FTEs) and utilized project management led by a single point of contact PM, based in the US. A single hit was provided by the client for each program. These programs were geared toward increasing potency and improving upon suspected pharmacokinetic (PK) issues. The US based AMRI Computer Aided Drug Discovery group also was utilized to identify a small focused library from our own chemical collections to further expand the scope of the initial SAR. Utilizing this information, the project manager designed a work plan from which the Indian team quickly expanded the SAR profiles for both hits with the syntheses of approximately 200 analogs over 13 months (averaging 4–7 linear steps each). *In vitro* biological results provided by the client identified a lead compound which had a 100-fold increase in potency over the initial hit for one of the programs. Several AMRI scientists were listed as co-authors on two peer-reviewed journal articles submitted by the client.

Case Study 2.
AMRI is producing a lead oncolytic API, currently moving into Phase III clinical trials, for a leading specialty pharmaceutical company. AMRI has supported the program for the past three years, beginning with the first toxicology supplies. Using our global resources, AMRI conducted process and analytical development jointly between the Indian (Hyderabad) and US teams. AMRI's Aurangabad Indian team has successfully scaled to ~100 kg batches of key intermediates at competitive low cost which have been converted into final API at AMRI's US manufacturing facility. Employing this strategy has allowed AMRI's customer to develop a reliable and competitive supply chain while concurrently providing the desired proximity of the final manufacturing within the US.

Space does not permit a more in-depth examination of these or the many other examples of globally integrated projects where AMRI has been able to undertake blending its different locations. A cornerstone of our strategy has been to utilize AMRI operations in India to provide a foundation for global projects conducted at multiple locations. Although we experienced multiple challenges around culture and country logistics, today AMRI has over five years experience in integrating our global assets into a cohesive, integrated and reliable offering. As the marketplace continues to refocus on performance and price as equal partners in outsourcing decisions, AMRI is uniquely qualified to offer Western values and Western performance metrics at competitive pricing.

As the industry continues to evolve at what appears to be an increasingly rapid pace, it is difficult to predict what it will look like 20, ten or even five years from now. But in this era of globalization and a flattening of resources and capabilities, it is clear that opportunity exists for outsourcing companies to continue to improve how they conduct their business and thus gain further market share. As a partner to our customers in their quest to discover and develop new medicines, AMRI's hybrid, globally integrated model provides a competitive advantage, that is focused on driving true value for our customers, defined as new products identified and developed towards the market, at competitive cost.