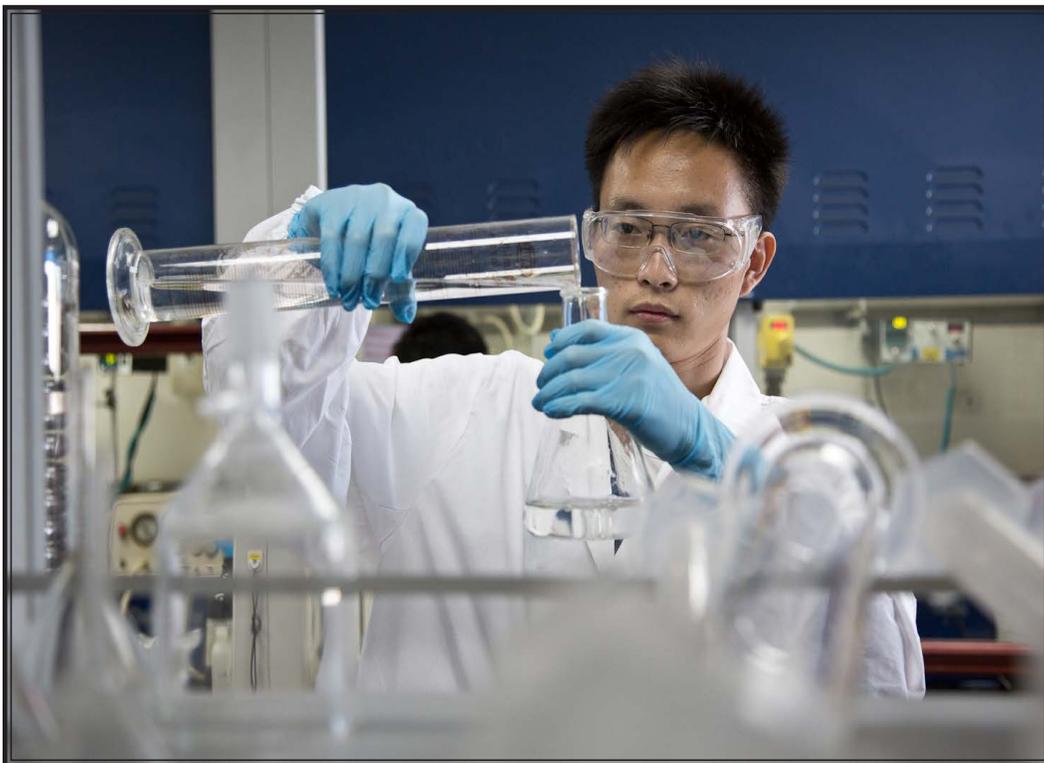


A Chinese Pharmaceutical Startup Acquires an American Firm to “Go Global”

June 2016



Preface

For decades, bilateral investment has flowed predominantly from the United States to China. But Chinese investments in the United States have expanded considerably in recent years, and this proliferation of direct investments has, in turn, sparked new debates about the future of US-China economic relations.

Unlike bond holdings, which can be bought or sold through a quick paper transaction, direct investments involve people, plants, and other assets. They are a vote of confidence in another country's economic system since they take time both to establish and unwind.

The Paulson Papers on Investment aim to look at the underlying economics—and politics—of these cross-border investments between the United States and China.

Many observers debate the economic, political, and national security implications of such investments. But the debates are, too often, generic or take place at 100,000 feet. Investment opportunities are much discussed by Americans and Chinese in the abstract but these discussions are not always anchored in the underlying economics or a realistic investment case.

The goal of the Paulson Papers on Investment is to dive deep into various sectors, such as agribusiness or

manufacturing—to identify tangible opportunities, examine constraints and obstacles, and ultimately fashion sensible investment models.

Most of the case studies in this Investment series look ahead. For example, our agribusiness papers examine trends in the global food system and specific US and Chinese comparative advantages. They propose prospective investment models.

But even as we look ahead, we also aim to look backward, drawing lessons from past successes and failures. And that is the purpose of the case studies, as distinct from the other papers in this series. Some Chinese investments in the United States have succeeded. They created or saved jobs, or have proved beneficial in other ways. Other Chinese investments have failed: revenue sank, companies shed jobs, and, in some cases, businesses closed. In this sense, past investments offer a rich set of lessons to learn.

Damien Ma, Fellow and Associate Director of the Paulson Institute think tank, directs the case study project.

For this case study of WuXi AppTec, we are grateful to James Harter, a talented University of Chicago graduate and student fellow at the Paulson Institute, for his excellent research and continued dedication.

Case studies are reconstructed on the basis of the public record, personal interviews with participants, and journalistic accounts. They aim to reflect a best reconstruction of the

case. But they may have gaps and other inadequacies where the record is incomplete, facts are murky, or players chose not to share their views.

Cover Photo: WuXi AppTec

Timeline

- 1982** From a basement in Minneapolis, Bonnie Baskin, a PhD in microbiology, launches ViroMed Inc., a medical diagnostic testing firm and the precursor to AppTec Laboratories.
- 1993** A team including Drs. Ge Li and John J. Baldwin, both PhDs in organic chemistry, establishes Pharmacopeia Inc., a provider of pharmaceutical R&D outsourcing in discovery chemistry.
- 1999** Li and Baldwin find a Chinese joint venture (JV) partner in Wuxi-based Jiangsu Taihushui Group Company. A skeptical board rejects their proposal.
- 2000-2001** Li, Baldwin, and three Chinese partners establish WuXi PharmaTech (WX) in Jiangsu province with the backing of Jiangsu Taihushui Group Company, offering combinatorial chemistry services to pharmaceutical companies.
- 2001** After US-based LabCorp acquires ViroMed's core diagnostic and cell culturing segments for \$40 million, Baskin spins off medical device testing and toxicology R&D outsourcing segments into a new company called "AppTec Laboratory Services."
- 2003** AppTec builds a new facility in Philadelphia for bio-pharma manufacturing, biologics safety testing, and cellular therapeutics.
- 2005** WX accepts a first round of foreign venture capital in preparation for an initial public offering (IPO) on the New York Stock Exchange (NYSE).
- 2006** WX expands beyond discovery chemistry and establishes its biologics division.
- 2007** WX lists on the NYSE for \$14/share, its stock price doubles within a month.
- 2008**
- January* WX uses IPO proceeds to purchase AppTec Laboratory Services.

- June* Covance, the US-based contract research outsourcing (CRO) giant, agrees but then reneges on a JV with WX to conduct preclinical CRO services in China.
- July* WX's stock price collapses, but private equity giant Warburg Pincus steps in to acquire a minority stake in the company.
- September* The financial crisis has significant effects on the global biotech industry: over the next three years, fully one quarter of all publicly listed biotech companies either cease to operate or are acquired.
- December* WX announces it will discontinue bio-pharma manufacturing in Philadelphia, laying off around 100 employees; WX writes down most of the acquisition's value for accounting purposes.
- 2010** Charles River Laboratories fails in its \$1.6 billion attempted acquisition of WX.

Key Players

United States

John J. Baldwin

Organic chemist, pharmaceutical industry veteran, and serial entrepreneur; plays a key role in establishing Pharmacoepia and WX

Bonnie Baskin

Microbiologist and founder and CEO of ViroMed and AppTec Laboratories

AppTec Laboratory Services Inc. (“AppTec”)

Minneapolis-based provider of biotechnology and pharmaceutical research and development (R&D) services outsourcing

Pharmacoepia Inc. (“Pharmacoepia”)

Pioneering contract research outsourcing firm based in Princeton, New Jersey

China

WuXi PharmaTech Corp. (“WX”)

The first and largest China-based provider of pharmaceutical and biotechnology R&D outsourcing

Jiangsu Taihushui Group Company

Chinese conglomerate and early funder of WX, based in Wuxi City, Jiangsu province

Ge Li

Organic chemist, founding scientist at Pharmacoepia, and Chairman and CEO of WX

Introduction

During the last week of November 2015, US presidential hopefuls on opposite sides of the political spectrum, Democrat Bernie Sanders and Republican Donald J. Trump, struck a rare note of shared outrage. Both candidates were said to be incensed over the intended merger of drug giants Pfizer and Allergan—a merger that valued Allergan at over \$160 billion.¹ In March 2016, alleging “tax avoidance,” Sanders wrote to the Treasury Department demanding that it block the deal.

The announced deal would have been the largest pharmaceutical merger in history, creating the world’s fourth largest company by market value, behind only Apple, Alphabet (Google), and Microsoft. What particularly irked the two candidates was the post-merger plan to relocate the new company to Dublin, Ireland, the home of Allergan. Pfizer, of course, had been based in New York for 166 years.

But since Ireland has a much lower corporate tax rate than the United States, Pfizer and Allergan were in apparent pursuit of an effective tax rate for the new company that would be

closer to 17 to 18 percent, well below Pfizer’s 25.5 percent effective tax rate in 2014 and 27.4 percent in 2013. The merger would have meant enormous tax savings, considering that the company paid \$3.12 billion and \$4.31 billion in taxes in 2014 and 2013, respectively.²

Throughout 2014 and 2015, a flurry of similar “tax inversion” deals took place across a number of industries, but news of the Pfizer-Allergan merger

came as a surprise because the Obama Administration had only just issued new rules intended to make inversions harder to accomplish and less profitable. Once the US Treasury Department released the new

rules, several large inversion deals were actually scrapped, including a \$54 billion deal between two other pharmaceutical giants Abbvie and Shire.³ (Pfizer’s merger ultimately floundered for the same reason.⁴)

Sanders blasted the deal as an “unpatriotic” ploy to evade taxes and “a disaster for American consumers,”⁵ criticizing Pfizer’s recent employment and research practices and charging that “Pfizer has slashed its workforce in

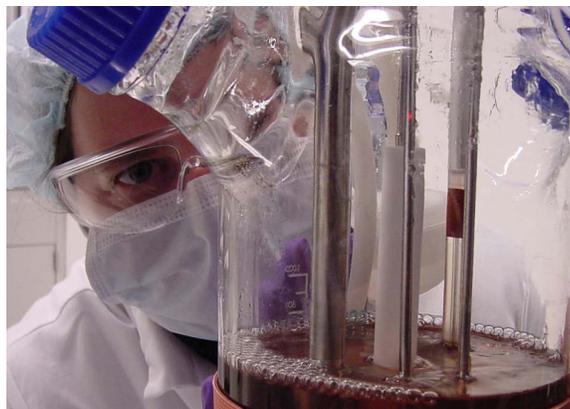


Photo: WuXi AppTec

recent years. It has repeatedly cut its research budget in favor of acquisitions and other profit-driven maneuvers.” Trump echoed Sanders’ sentiment on potential job losses, fulminating that “the fact that Pfizer is leaving our country with a tremendous loss of jobs is disgusting.”⁶

Other politicians piled on too, including Democratic presidential frontrunner Hillary Clinton, Senate Democratic leader Harry Reid, and Republican Senator Orrin Hatch, chairman of the Senate Finance Committee.

In fighting back, Pfizer’s CEO Ian Read claimed that synergies and tax savings from the deal would allow the two companies to preserve, not shed, their research and development (R&D) operations in the United States. The merger, he argued, “allows us to continue to sustain an investment of approximately \$9 billion mainly spent in the United States,” adding, “we have 40,000 combined employees in the United States.”⁷

But Read’s claim was met with skepticism against the backdrop of Pfizer’s historical record and secular trends in the pharmaceutical industry. Pfizer’s last major acquisition had occurred in 2009, when the company bought Wyeth for \$68 billion. Before the merger, in 2007, Pfizer’s R&D spending was \$7.8 billion and Wyeth’s around \$5 billion. By 2013, Pfizer had cut the R&D budget of the combined company to

just \$6.55 billion.⁸ This meant layoffs—between 2008 and the end of 2013, Pfizer shed about 51,500 total jobs.⁹ Why does this background matter to a Chinese acquisition in the United States? The answer lies in what it says about underlying changes in the global pharmaceutical industry.

Mega deals like Pfizer-Allergan invariably attract the spotlight and invite political controversy. Yet Pfizer’s move was part and parcel of a larger shift in an industry that has been slashing its R&D budgets and workforce for years. For example, AstraZeneca cut some 13,500 jobs during the same timeframe. Merck shed about 24,000 jobs from 2009 to 2013 following its acquisition of Shering-Plough.¹⁰ Indeed, over a ten-year period beginning in the early 2000s, the US pharmaceutical industry is estimated to have laid off a total of more than 300,000 people.¹¹

This trend poses different challenges from job losses seen in more traditional industrial sectors across the United States. Unlike the outsourcing and automation of low-skilled jobs in manufacturing, for instance, the jobs disappearing from the pharmaceutical sector are well paid and require advanced degrees. These are precisely the types of high-skilled jobs that have been assumed to be “safe” for American workers from the twin forces of globalization and automation that have radically altered some industries and regions of the United States.

How and why, then, did this happen? Put simply, a paradigm shift in drug discovery and development has caused vast labor force disruption. Unlike the “Golden Age of drug discovery” that took place after World War II, the pharmaceutical industry has experienced stagnant revenues, lower productivity, and higher costs over the past two decades.

The postwar period saw remarkable advances in chemistry and biology, which in turn led to the expansion of the industry and creation of important new intellectual property (IP). This was a period in which strong linkages were established between business and government in an effort to create new antibiotics and blood plasma products. That effort led to more R&D financing and investment, and pharmaceutical companies led the way in drug discovery and development, with outsourcing playing a very limited role.

But as the pharmaceutical industry approached a “patent cliff”—in other words, where revenues would decline dramatically as patents expired, allowing competitors to produce at lower prices—and sought to contain R&D costs in recent decades, companies adopted different strategies. These firms relied primarily on three methods, with some companies emphasizing one over the other and some individual companies

even prioritizing different strategies across different divisions.

The first and most prominent strategy has been to “merge and slash,” as was manifest in the proposed Pfizer-Allergan deal. It involves combining products, consolidating staff, and acquiring new treatments from upstart biotech companies reaching the later stages of the drug development process.

The second strategy centers on “open innovation.” Drug companies formed collaborative partnerships to shrink the divide between academic and industrial research. Their aim in doing so is to reduce the cost of drug discovery by pooling the risk of failure and eliminating duplicative research.

The third strategy—and the focus of this case study—is “reverse innovation” centered on the contracting of research from companies that once lacked the capabilities to do innovative science but now possess such capabilities at lower cost.

The contract research and contract manufacturing outsourcing (CRO and CMO) model has emerged as the most popular strategy for the industry. Rather than do all their work internally, drug companies have for some time now outsourced R&D to specialty companies, most of which are located in the United States and Western

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Europe and were founded by ex-pharma executives and scientists.

In fact, many of the 300,000-plus jobs that major drug companies cut did not disappear entirely; rather, they simply moved to CROs and small biotech companies that were developing new treatments in the hopes of one day finding a big pharma firm as buyer. As a result, the CRO industry in the United States has grown exponentially.

Even as the CRO industry expanded in the United States, it has also experienced dynamic change over the past 15 years. After a strong start in America, many of the CRO jobs shifted from the United States and Western Europe to India and China, two countries that became major players in drug discovery and development.

These two Asian giants have lower costs, relatively educated workforces, and governments eager to strategically develop domestic healthcare and pharmaceutical industries. Almost every large CRO and pharmaceutical company has capitalized on these factors to shift varying portions of their R&D operations to one or both countries.

Moreover, Indian and Chinese citizens, educated and/or trained in US and European universities, have also returned home to set up their own CRO/CMO companies. A few of these companies have grown in size and reputation and now rival their Western

competitors. More recently, Indian and Chinese firms have begun moving beyond research outsourcing toward local drug discovery and development. A number of small biotech firms trying to find novel treatments for diseases have sprouted up, especially in China.

As domestic Chinese and Indian CROs have grown and matured—and as foreign competitors have built their own operations in those two countries—Asian and US/European operations and strategies appear to be converging. For instance, many Indian and Chinese companies have established joint ventures (JVs) with their Western counterparts and built or acquired operations in the United States and Europe. In similar fashion, Asian firms have been acquired by their US competitors that are eager to expand into China.

One such Chinese company is WuXi PharmaTech (“WX”). Founded in China in 2001, WX acquired a US-based firm, AppTec Laboratories, in 2008 for \$163 million. WX then built on this foundation with numerous subsequent acquisitions in the United States, as well as both successful and failed JVs with US CROs, such as Pharmacopeia and Covance. A US firm, Charles River Laboratories, failed in its \$1.6 billion bid for the company in 2010. In short, WX’s story captures the rapid pace of evolution in the CRO and pharmaceutical industries over the past 15 years.

WX's acquisition of AppTec must be seen within the context of the dramatically changed landscape of pharmaceutical and biotech R&D and innovation: The R&D paradigm for new drugs and treatments has evolved from vertical integration within a single, large pharmaceutical firm to become more horizontally linked through partnerships with CROs. Over the past two decades, research outsourcing companies have moved to capture the talent arbitrage opportunity between the United States and Asia by offshoring many of their testing and manufacturing operations.

China has been an especially big beneficiary of the growth of the global CRO industry. And in that sense, WX's investment was not necessarily unique in the context of broader industry dynamics, but was significant because it involved a Chinese firm that was the first China-based CRO to specialize in discovery chemistry services.

Like all firms in the pharmaceutical industry, WX has had to adapt to shifting winds and keep up with technological and economic changes. The CRO space has become fiercely competitive, as companies have vied to expand their service offerings and make more stages of the R&D process available for outsourcing. This race to become fully integrated providers

has yielded both rapid growth and consolidation of firms in the CRO industry.

For WX, these trends meant that the firm would organically grow its service offerings where it could. Ultimately, WX decided to pursue the AppTec acquisition in the United States to expand in areas that it deemed too difficult to develop internally. This case study explores WX's history and acquisition of AppTec in 2008. It provides an analysis of WX's spectacular growth and success in China, the

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motivations behind its decision to invest in the United States, and suggests some potential lessons that can be drawn for

investors seeking to target the R&D and innovation realm.

At a broader level, the case helps to illuminate how economic and market changes have profoundly affected the global drug discovery and development machine responsible for advances in healthcare, pharmaceuticals, and government-sponsored research over the last few decades.

Key Takeaways

The case illustrates several lessons:

- In the past, most attention to outsourcing from America to lower-cost markets has focused on low-

skilled manufacturing jobs. But this case shows that similar trends are and will continue to occur in high-skilled industries, including in healthcare research and software programming. The trend towards outsourcing more high-skilled labor will likely accelerate as universities in China and India continue to graduate large numbers of students across STEM disciplines.

- Essential to WX's early success was its ability to effectively leverage the work experience and connections of its founders. This enabled it to win business from US and European clients. As China seeks to expand its services economy, then, winning trust by leveraging international educational credentials, professional experience, and customer relationships will continue to be crucial for Chinese firms in their effort to attract global customers.
 - To be branded as an "international" company rather than a "Chinese" firm proved to be very important to WX and other Chinese CROs. WX was keen to brand itself as a reputable, independent, and international operator. Several of its key decisions, such as accepting venture capital (VC) money from Fidelity and Singaporean banks, choosing to go public in the United States rather than in China, and the acquisition of US-based AppTec, were deeply influenced
- by management's strategy to gain credibility and respect from the international scientific and business communities.
- Highly technical services can be difficult to develop organically. That is because the procedures, expertise, and customer relationships they require are substantial and onerous. An upstart company such as WX may turn to mergers and acquisitions (M&As) to expand its service offerings.
 - Large drug companies have had to adapt to tough macroeconomic conditions and globalization, but the proliferation of CROs and biotech startups has made it easier than ever for a scientist with a promising idea to strike out on his or her own and establish a niche.
 - WX learned that attempts to cross-sell AppTec's services to WX's pharmaceutical clients took longer than anticipated. This was particularly true of AppTec's biologics manufacturing business. Some reasons included difficulties in convincing large, bureaucratic pharmaceutical clients to move quickly to outsource new functions. WX's challenge was greatly amplified by deteriorating economic conditions—these prompted the companies to undertake drawn-out strategic reviews of their operations.

The Great Global Pharma Disruption

For most of the past two centuries, the pharmaceutical industry has been concentrated in three advanced markets: the United States, Western Europe, and Japan. In the United States, modern pharmaceutical companies began emerging as early as the late 1800s, many of them starting out as drug store chains that subsequently expanded into the supply and production of drugs and elixirs. Familiar names today such as Pfizer and Bristol-Meyers Squibb date back to this period.

Western Europe traces its own pharmaceutical industry to the evolution and combination of dye, apothecaries, and chemical suppliers over the course of centuries. But it was in the late 19th

century that German and Swiss companies began entering the US market. As part of the wartime policies in the first (1914-18) and second (1941-45) World Wars, the US government confiscated these companies' US operations and spun them off as independent enterprises, creating Merck & Co. and Schering-Plough, among others.

In Japan, the pharmaceutical industry dates back to traditional herbal medicine sellers, with its modern

incarnation coming of age during the nation's rapid period of industrialization and transition to Western medicine and modern corporate structures in the interwar years.

The World War II effort was a major catalyst for drug discovery in the United States, bringing together businesses and government to create new antibiotics, blood plasma, and other treatments for the armed forces. Both public spending and private capital were eager to



Photo: Flickr/Oliver Dodd

finance drug R&D. In the postwar period, the implementation of socialized medicine in Europe and the proliferation of private health insurance in the United States expanded healthcare access to more

people than ever before. As a result, the pharmaceutical industry began aggressively marketing new drugs and treatments to patients. No such marketing existed prior to World War II.

This so-called "golden age" led to huge advances in chemistry, biology, and the expansion of the industry. Such an era was made possible because of the association between large and productive pharmaceutical companies, elite research

universities training the next generation of scientists, and a federal government willing to support innovation.

During this period, the United States became the world's most important pharmaceutical powerhouse, producing over half of the world's drugs. With research advances in chemistry, biology, and synthetic chemistry, major successes were achieved in helping to control chronic long-term diseases and enable people to live longer and healthier lives. For instance, products such as synthetic vitamins, sulfonamides, antibiotics following penicillin, and antihypertensive agents began to reach patients and changed the approach to treating cardiovascular disease.

Significant progress was also made during the 1960s-1980s, when the advent of mechanism-based drug design created treatments for diseases such as Parkinson's and high cholesterol, and led to breakthroughs in chemotherapy and oral contraceptives. As the HIV/AIDS epidemic caught the attention of major governments around the world, the period from 1980-2000 saw tremendous efforts placed on anti-viral research. In recent years, breakthroughs in anti-viral treatments changed HIV/AIDS from an automatic death sentence to one that could be managed through chronic therapy.

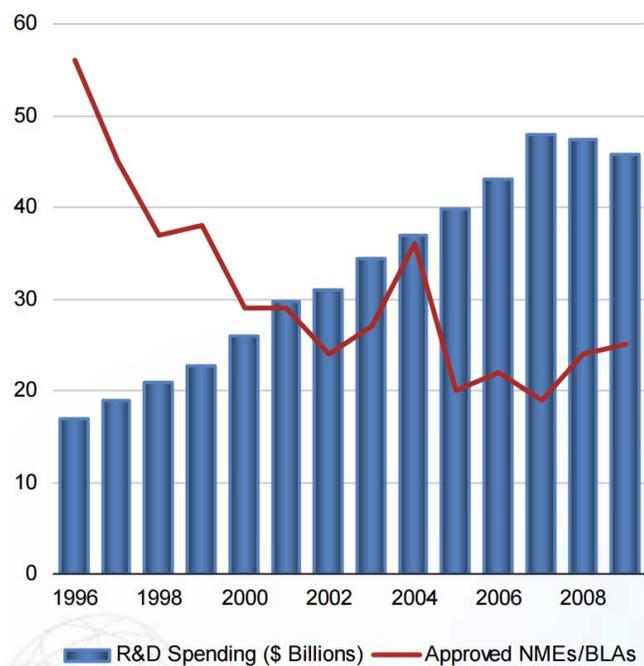
Another significant discovery during this period was treatment for River Blindness in Africa, a disease once

thought too prevalent to tackle but is now on course for complete global eradication. The biotechnology sector also emerged during this period, which represented an entirely new research and discovery business model outside the traditional pharmaceutical industry that could also contribute greatly to human health.

At the same time, pharmaceutical companies began to see that it was increasingly costly to develop new entities useful in therapies. Research costs were rising, and the time it took to take innovative science and convert it into therapeutic agents grew longer. Drug approval times increased, and existing drug products that had provided the fuel to drive investments in R&D gradually ran out of patents.

These trends became a major problem because pharmaceutical companies' valuations rise and fall with the discovery and patent expirations of the new chemical entities (NCEs) used to make drugs. Further, governments in the United States and elsewhere, which earlier had been very supportive of the pharmaceutical industry, began to withdraw their support as they confronted long-term entitlement and fiscal challenges. As a result, whether the state's historic support for drug R&D would persist began to be called into serious question (see Figure 1).

Pharmaceutical companies initially responded to these headwinds by

Figure 1. Declining Productivity of Pharmaceutical R&D Spending

Source: WuXi PharmaTech Investor Presentation.¹²

seeking new technologies to lower the overall cost of drug discovery by making it more productive and reducing the time length of discovery. Innovative new methods such as computational design, combinatorial chemistry, high throughput screening, macromolecular x-ray crystallography, informatics, genomics, and others were developed for this purpose and became integral methods for drug discovery today.

By the early 1990s, a number of leading pharmaceutical companies also faced patent cliffs as many patents approached expiration. To cut costs, affected companies offered early retirement incentives to senior scientists and laid off junior staff.

Such actions marked a new era in the employer/employee relationship in the pharmaceutical industry. Previously, there had existed what essentially amounted to a researcher's lifetime commitment to a single pharmaceutical company, and a belief that such a commitment to the contract would be honored.

Some of those employees, armed with rich insider knowledge of the industry and the drug innovation process, had other ideas.

Changing Business Models

John J. Baldwin, an organic chemist at Merck & Co, was one such employee offered an early retirement package.

As a senior scientist and manager of Merck Research Laboratories, Baldwin had a productive and distinguished 33-year career that included the development of several path breaking and profitable drugs. He is the holder of more than 180 US-issued patents and has been inducted into the Medicinal Chemistry Division Hall of Fame. Instead of settling for retirement, however, Baldwin struck out to become an entrepreneur.

During Baldwin's time at Merck, the company released several drugs to his personal credit, including two for the treatment of glaucoma, Trusopt and Cosopt. Baldwin also made important contributions to a wide range of therapeutic areas, including cardiovascular medicine with Aggrastat, HIV/AIDS treatment with Crixivan, and played a key role in developing Pepcid, a blockbuster drug for heartburn and indigestion. Pepcid, of course, went on to generate billions in revenue for Merck and became a widely available over-the-counter drug.¹³

As Merck was offering early retirement incentives, Baldwin at the same time began exploring other options. He and some of his peers became interested in research conducted at Columbia University and Cold Springs Laboratory by scientists Clark Still and Michael H. Wigler, respectively. The researchers were developing techniques in the early-stage drug discovery process that would prove to have market potential.

In the past, a major bottleneck in the drug discovery process involved the limited number and diversity of available chemical compounds. Using traditional manual chemical synthesis techniques, a chemist is usually able to synthesize 25 to 50 compounds per year. These compounds are screened in order to select potential leads for drug candidates.

Over the years, however, several technologies were developed to accelerate the synthesis of chemical compounds, but most of the earlier methods produced high molecular weight compounds that are generally considered not useful for oral drugs. Pharmaceutical companies prefer low molecular weight compounds because they are more likely to be effective as drugs in tablet or capsule form, tend to have longer-lasting action, and are cheaper to manufacture. High molecular weight compounds are usually degraded by human digestive enzymes and must be administered by injection.

The techniques Still and Wigler developed, called "Encoded Combinatorial Library on Polymeric Support" (ECLiPS), enabled researchers to quickly generate hundreds of thousands of small molecule compounds at a fraction of the cost of traditional chemical synthesis methods.¹⁴ The new technology unleashed the potential to harness recent advances in combinatorial chemistry, which involved the synthesis of large numbers of different chemical compounds by creating all possible combinations of

a set of chemical components, or the building blocks of a new drug. These compounds can then be tested for potential drug candidates in a process called “high-throughput screening” (see Box).

Still and Wigler’s efforts unlocked the tremendous potential of “pool and split” for research purposes and simultaneously reduced the cost and time required to generate leads for new drug candidates. But the technique

Box: Accelerating the Drug Discovery Process

Existing approaches to combinatorial chemistry required inducing huge numbers of chemical reactions. For example, a robotics-based method developed and popularized in the 1980s called “parallel synthesis” needed approximately 111,110 individual chemical reactions to synthesize 100,000 compounds. A newer approach, called “pool and split,” dramatically slashed that number to only 50 chemical reactions to synthesize the same 100,000 compounds.¹⁵

“Pool and split” had the potential to drastically cut the labor, time, and capital investment that techniques like parallel synthesis required. However, “pool and split” produced a serious complication: it created a mixture of diverse compounds whose structures all need to be determined to be useful for research. The methods available to do so were slow and labor-intensive. Determining the structure of just one of those 100,000 compounds produced in the mixture could take several weeks of a research scientist’s time.¹⁶ Consequently, Still and Wigler’s ECLIPS was the solution to accelerate this process, as it permitted rapid identification of compounds synthesized by “pool and split.”

The first component of the method isolated the individual compounds with a technique called “solid phase synthesis.” Instead of synthesizing the compounds in a liquid solution, the solid phase process synthesized compounds on tiny plastic beads. Compounds are bound to these tiny plastic beads using special linkers. Beads are then washed with solvents to remove byproducts, and individual compounds can then be isolated from a mixture by removing a single bead and breaking the linkage to detach the compound from the bead.

The second component overcame the challenge of identifying the compounds. During each step of the solid phase synthesis process, specific tags are attached to each bead to indicate the chemical reagent and reaction conditions used in that step. By the end of the synthesis process, each bead has accumulated a set of tags that represent all of the building blocks used to create the compound on that build. Using the tags, researchers can then quickly identify the structure of an active compound using the “pool and split” technique. The results are captured and stored in a database for active compounds.

was so cutting edge and new that pharmaceutical companies had not yet adopted it when Baldwin started exploring these new methods. Baldwin and his colleagues believed that these advantages were exactly what pharmaceutical companies needed to be able to reshape early-stage drug discovery.

In 1993, after reluctantly accepting the early retirement package, Baldwin joined several of his Merck colleagues in an effort to commercialize ECLiPS, including Joseph A. Mollica, the former Chairman and CEO of Merck's JV with DuPont Chemical Company, John Chabala, Merck's former Executive Director of Basic Chemistry, and Nolan Sigal, Merck's former Executive Director of Immunology Research.

The group entered into an exclusive license agreement with Columbia University and Cold Springs for their patent applications covering molecule encoding. Several of Still's PhD students at Columbia also signed on to the venture, including Ge Li, a Chinese national who had just earned his doctorate in chemistry at Columbia in 1993.

New Startup Formed

In March 1993, the group established Pharmacopeia Inc. in Princeton, New Jersey. Unlike traditional pharmaceutical firms, Pharmacopeia had no plans to develop, manufacture, and sell its own products. Rather, the company's strategy

was to provide collections of compounds and drug development candidates to pharmaceutical and biotechnology customers using the ECLiPS technology. The company's customers would be responsible for the clinical development and eventual manufacture and sale of resulting drugs. Baldwin assumed the role of Pharmacopeia's Senior Vice President of Chemistry.

Pharmacopeia tailored its services to the individual customer's needs within three broad frameworks: forming drug discovery collaborations, licensing libraries, and out-licensing compounds from internal discovery programs. The first two are the most important and proved to be the most successful. "Drug discovery collaborations" meant that a pharmaceutical company would hire Pharmacopeia to synthesize targeted and optimized libraries of compounds and conduct high-throughput screening to identify drug development candidates in the libraries.

For example, in December 1994 Pharmacopeia signed its first collaborative agreement with Schering-Plough, in which Schering-Plough tasked Pharmacopeia with synthesizing and optimizing libraries of lead compounds that interact with molecular targets related to cancer and asthma. As for "licensing libraries," Pharmacopeia would continuously add to its own set of internal compound libraries, to which customers could pay for access. With access, customers would themselves

screen compounds for potential drug lead candidates at their own facilities using Pharmacopeia's internal libraries.

As a startup, Pharmacopeia was a unique entrant into the rapidly emerging CRO industry. At the time, most CROs primarily served smaller biotech companies, and to the extent that they worked with big drug companies, it mainly focused on later stages of the drug development process such as preclinical and clinical trials. Pharmacopeia was unusual in that its services were (1) for early-stage drug discovery and (2) targeted to serve large pharmaceutical companies.

This was a break from historical practices, where drug companies conducted early-stage discovery entirely within their own research departments. Factors such as the highly proprietary nature of the work, the central importance of the activities to their drug discovery and development efforts, and

the desire to obtain maximum patent and other protection of their internal programs all argued for the more vertically integrated model.

To convince these very large and sophisticated clients to take the unusual step to outsource parts of the early-stage drug discovery process to a third-party startup, Pharmacopeia needed more than just the impressive ECLiPS technology. Ultimately, the reputations, connections, and achievements of the startup's management and scientific teams were indispensable factors in sealing some significant deals, despite the lack of industry precedent.

In fact, the company quickly signed up major customers, including Schering-Plough, Sandoz, Bayer, and the Japanese pharmaceutical company Daiichi. Its initial success led Pharmacopeia to list publicly on NASDAQ in December 1995—less than three years after its inception.

The CRO Boom

The existence of the CRO industry is predicated on the simple premise that certain products, testing, and services can be more efficiently provided by third parties, even in the sophisticated and technology-intensive field of pharmaceutical research.

During the 1980s and 1990s, CROs were riding on the coattails of the biotech boom. Unlike large and diverse pharmaceutical companies, biotech startups generally have a specific expertise and research focus, such as novel lead generation methodologies and understanding of a disease's models and pathways. They are generally much smaller and may have a predetermined operational lifespan for the company in mind. As such, biotech firms often lack the resources to develop the full spectrum of capabilities needed to execute every stage of drug discovery and development internally, which would require significant investments in capital expenditure for laboratories, manufacturing, human capital, and other preclinical and clinical testing capabilities.

To fill these gaps, biotech firms must outsource services to third parties, and as the biotech industry soared, a number of CROs were established to serve them and grew into significant

companies earning hundreds of millions of dollars in annual revenue, such as Quintiles, Parexel, and PPD.

Although CROs had existed for decades prior to the proliferation of biotech, they had served only a supporting role during the later stages of the drug development process, such as conducting preclinical and clinical trials in animals and humans. Such trials require complex permitting, breeding, sales, and upkeep of exotic lab animals and finding a sufficient number of humans with the desired characteristics for trials.

The existence of the CRO industry is predicated on the simple premise that certain products, testing, and services can be more efficiently provided by third parties.

For a long time, researchers had recognized the benefits of outsourcing some

of that type of work to specialized companies. Not surprisingly, therefore, many of the oldest CRO companies that existed prior to the biotech boom originated in the business of laboratory animals, the most prominent ones being Covance and Charles River Laboratories.

Animal Testing and CROs

A young veterinarian named Henry Foster founded Charles River Laboratories shortly after the end of World War II. Foster anticipated that all the new money being pumped into the Boston/Cambridge area's elite university

research laboratories would create healthy demand for lab animals. In 1947, Foster had thousands of rat cages that he had purchased from a defunct Virginia farm shipped up to a rental by the Charles River in Boston and began breeding rats. (Rodents are widely used in medical research because they have immune systems similar to humans and reproduce rapidly.)

From its unremarkable beginnings, Charles River Laboratories slowly grew and broadened its services over the ensuing decades into toxicology, preclinical, and clinical testing.¹⁷ It became a pioneer in commercializing transgenics when, in 1987, the company started selling transgenic mice that had been gene spliced at the embryo stage to produce a particular desired trait.¹⁸

Covance, on the other hand, traces its roots back to a grocery store's basement in Seattle, Washington in 1968, where a team manufactured equipment used with laboratory animals. Over the years, the company expanded its services to include breeding and selling lab animals, toxicology testing, preclinical and clinical development services, and cell culturing, primarily serving the biotech industry.

The company gained international notoriety in 1989 when primates in its Reston, Virginia testing facility were found to be infected by the deadly Ebola virus. Because of the facility's close proximity to Washington, DC, the incident attracted a tremendous

amount of global attention and was subsequently dramatized in the best-selling nonfiction thriller *The Hot Zone* by Richard Preston. Nevertheless, Covance recovered from the crisis and continued to grow. By 1998, it had net annual revenue of \$732 million.¹⁹

The New Paradigm: Outsourcing R&D

As market pressure mounted on the pharmaceutical industry in the 1990s, drug companies began outsourcing a small but sizable portion of their R&D activities to these CROs. By 1997, four years after the founding of Pharmacoepia, 37 percent of US pharmaceutical companies outsourced at least some R&D projects. This translated into about \$2 billion—or 10 percent of the US pharmaceutical industry's total R&D spending in 1997—a significant portion of their R&D spending but still less compared to biotech firms.²⁰

In Western Europe, the R&D paradigm was disrupted earlier, which included both using CROs for preclinical and clinical trials and relocating internal R&D operations to other markets. For instance, in 1990, as much as three quarters of European pharmaceutical companies' R&D budgets were allocated domestically. That proportion had dropped to under 60 percent by the end of the decade.²¹

Government policies, particularly price controls on prescription drugs, had

an impact on the increasing trend of outsourcing. Throughout the 1990s and 2000s, healthcare spending in Western European countries soared, in part because the government provided partial or total reimbursement for the cost of prescription medicines. At the same time, most governments also resorted to price controls to curtail runaway government spending on entitlement benefits that cover prescription drugs.

Such policies had the cascade effect of hitting company revenues, which led to R&D funding cuts and increasing pressure to contain drug development costs. Many European pharmaceutical companies ended up shifting sales and R&D activities to the United States, where drug prices were still more market based.²²

While business was heating up for many CROs in the late 1990s, Pharmacopeia's chemistry discovery business was slowing. Within a few years of Pharmacopeia's launch, nearly all drug companies had adopted theirs or a comparable approach to generate large screening collections. What had been deemed cutting-edge technology not so long ago very quickly became a common basic requirement within every drug discovery organization.

By 2000, Pharmacopeia had grown to 746 employees, about 40 percent of which were chemists, biologists, and engineers with PhDs, and the discovery

chemistry segment was pulling in \$39 million in annual revenue.²³ Baldwin, who by then had taken on greater responsibility as Chief Science and Technology Officer, knew the company needed a new direction for its discovery chemistry segment.

"As times changed, really the only advantage that Pharmacopeia had in selling what had become a commodity was price and its experience in drug discovery," Baldwin recalled in an interview.²⁴

Making these compounds into libraries is very labor intensive. It is a complex chemical process performed repeatedly with different reagents to produce different compounds. A researcher can easily have 200,000 different compounds all in the same pot. Each of those little particles is then encoded with coding molecules. This allows for the compound to be identified easily, as the coding molecules are removed, which tells the researcher what steps that bead has been exposed to. The process requires a great deal of hands-on work, which is expensive.

"One obvious solution to the price issue was to move compound production to a lower-cost environment," Baldwin added.²⁵ In fact, some drug companies and CROs had already begun pursuing this idea, although they worked on different stages of the drug discovery and development process from Pharmacopeia's own specialization.

In particular, countries in Eastern Europe and India had been experiencing an influx of pharmaceutical companies and CROs. Those two regions had a labor pool that was considered skilled relative to the prevailing wage rates in those labor markets, creating what has been termed “talent arbitrage” opportunities. Exploiting this potential allowed CROs and drug companies to reduce R&D spending without sacrificing the quality of their research.

CRO/CMOs and pharmaceutical companies that shifted R&D activities to India benefited from lower wages, fewer regulations, and cheaper infrastructure such as IT support, and a large potential supply of patients for clinical trials.²⁶ Moreover, English is widely spoken in India, giving it an edge over other low-cost markets with language barriers that inhibit communication, which is crucial for these types of innovation-driven and knowledge-based firms. Studies showed that moving R&D to India could save multinationals anywhere between 30-50 percent in costs, depending on the service.²⁷

On the regulatory front, India was known, up until recently, as one of the easiest places to obtain approvals for

clinical trial proposals.²⁸ Since all clinical trials require human subjects, this was an important asset from the vantage point of CROs and drug companies. For most of the 20th century, these advantages were stifled by differences in disease profiles between the Indian and Western populations. But, over the past two decades, increasingly common “lifestyle” diseases in the West such as obesity, diabetes, and lung cancer have become much more prevalent in India, which has diversified its patient pool into more areas of study.



Photo: WuXi AppTec

These advantages turned India into a hotbed for clinical trials, as companies flocked there. In 1984, UK-based giant AstraZeneca opened an R&D center in Bangalore to support clinical

development and trials.²⁹ In 1997, North Carolina-based CRO Quintiles became essentially the first foreign CRO to enter the market when it began conducting clinical research. Quintiles grew into the largest CRO operation in India, growing to around 700 employees in three cities by the mid-2000s.³⁰

India also had a number of successful homegrown CROs, as returnees with overseas experience in Western companies rushed in to set up domestic competitors. A prominent example is Biocon—one of the first of these

firms—which dates back to 1978 when two scientists in Bangalore opened a makeshift “lab” in the garage of a rented house. They produced an enzyme used to prevent beer from appearing hazy and sold it to local brewers. Over the years, the company moved out of the garage and entered segments spanning biopharmaceuticals, biologics, and CRO businesses. Today, Biocon is India’s largest domestic biopharmaceutical company by revenue.³¹

Beyond clinical trials, India also emerged as a major player in manufacturing active pharmaceutical ingredients (APIs), which are commonly referred to as “bulk pharmaceuticals.” To cut costs, biotech firms, followed by pharmaceutical companies, have been winding down their internal API manufacturing and simultaneously ramping up outsourcing. For example, in 2009, AstraZeneca announced its intention to withdraw from all API production in favor of outsourcing to CMOs by 2016. At that time, the company still manufactured 85 percent of its own APIs.³²

In addition to India, Eastern Europe was also a growth market for CROs,

particularly for clinical trials. Since effective drug testing often requires the patient population to be genetically and racially similar to the intended final users, clinical trials for certain types of drugs tend to be conducted in the same region as where the customers are located.

Like India, Eastern Europe also had cost advantages because patient reimbursements were generally significantly lower than in the United States or Western Europe. For instance, in the early 2000s, compensation for volunteers and medical staff for clinical trials in Western Europe and the United States was typically around \$5,000 per person. By contrast, it only cost an average of \$2,000 per person in Bulgaria, Romania, and Croatia, so potential savings could be considerable.³³

As a result, during the 1990s and early 2000s, many leading CROs established bases in Hungary, Poland, and the Czech Republic. For example, Quintiles opened offices in Bulgaria, Russia, and Croatia, while ICON Group International and Parexel set up operations in Latvia and Lithuania.³⁴

China Enters the Pharma Outsourcing Game

Despite the rapid changes in the pharmaceutical R&D landscape, early-stage CROs such as Baldwin's remained relatively untouched by the outsourcing trend to lower cost markets. "Our methodology of encoding to predict structures was so novel," said Baldwin, "India wasn't doing anything like this."

As noted above, Baldwin did, however, hire a talented young Chinese chemist named Ge Li at Pharmacopeia. "He had just got out of his PhD at Columbia where he was a student of Clark Still. Ge Li and I decided, why not lower the cost structure by moving this hand work to China?"³⁵

With the blessing of Pharmacopeia's board, Baldwin and Li traveled to China in 1999 and met with a number of companies that they hoped could develop the capabilities and acquire the expertise to do their type of chemistry and would be willing to form an alliance with Pharmacopeia. This was a tall order at the time. After all, the kind of discovery chemistry needed for early-stage drug development did not even exist in China, so the two men cast a wide net in search of potential partners.

The entity they eventually found most promising was a state-owned conglomerate in Wuxi, Jiangsu province called Taihushui, which owned a diverse array of assets, ranging from beer breweries to horse racing tracks.

Most relevant for Pharmacopeia, however, was that Taihushui also had some experience in chemistry-related manufacturing: the company made and sold green tea extracts to the US food industry as an ingredient in

canned products. It also helped that Taihushui was very receptive to Pharmacopeia's proposal and expressed serious interest in investing in the US company.

The two men returned to New

Jersey convinced that relocating Pharmacopeia's early-stage discovery chemistry to China was both feasible and economical. They recommended that Pharmacopeia pursue an alliance with Taihushui to what was admittedly a skeptical board. China had yet to enter the World Trade Organization and emerge as the economic powerhouse of today, not to mention that a few of the board members had negative views on the China market.³⁶



Photo: Flickr/Gwydion M. Williams

Beyond this general skepticism of doing business in China, the company's board had also changed its primary focus from discovery chemistry outsourcing to molecular modeling and simulation software for the life sciences and materials research markets. That was because the tech boom of the late 1990s had led the company's software business to grow much faster, and it quickly eclipsed the discovery chemistry segment in total revenue.

For these reasons the board did not move forward on Baldwin and Li's proposal. The question became "what were we going to do with all this information we had learned [in Wuxi]?"³⁷

The two men could not let the idea go. With the eventual permission of Pharmacoepia's board, they traveled again to China to dig deeper. On that trip, they met with China's State Food and Drug Administration, Taihushui, and others to determine how much it would cost to establish an independent discovery chemistry outsourcing company.

"At that point in time, we decided, 'all right we're going to set up a company, and Ge Li is going to go over there and run it,'" Baldwin recounted. "When Pharmacoepia wasn't willing to spread out to China, we went back to Taihushui and did a deal with them."³⁸

"[Li] felt that the idea was so compelling that he had to do this on his own,"

added Hai Mi, a former investor relations representative at WuXi PharmaTech.³⁹

Striking Out on Their Own

Sensing that Pharmacoepia would be ultimately unwilling to take the risk, Li and Baldwin decided to take matters into their own hands. In early 2001, the two men, along with Chinese businessmen Xiaozhong Liu and Tao Lin and a Chinese marketing professional Zhaohui Zhang, established WuXi PharmaTech ("WX") using the founders' own savings and funding from Taihushui.

Li resigned from his job at Pharmacoepia to become CEO and Baldwin got permission from Pharmacoepia to sit on the new company's board. Li's wife, Ning Zhao, who had also received her doctorate in chemistry from Columbia, left her job at Bristol-Meyers Squibb soon after to join her husband at the new venture.

WX's equity was split into three blocks: ChinaTechs Inc., Jiangsu Taihushui Group Company, and Baldwin himself. The three parties held 55 percent, 39 percent, and 5 percent equity interests in the new company, respectively. The ChinaTechs stake was an investment vehicle split between WX's founders and other early employees.

The founders decided to locate the company in Wuxi, a city of over six million near Shanghai in order to be

close to Taihushui's headquarters. The company received generous support from the city government, including a very favorable land deal and some income and sales tax exemptions. However, it did not take long for WX to decide that it would rather move its headquarters into one of the trade zones located outside of Shanghai. That's exactly what WX did within a year, after selling the land it had received from the Wuxi government.

The startup spent much of 2001 hiring staff, building its facility, and establishing internal processes. In its first year, WX hired 48 employees, 27 of whom held doctorates. By March 2002, WX secured its first major customer Merck & Co., which incidentally counted several of Pharmacoepia's founders as alumni. WX's job was to prepare synthetic organic compounds and libraries on a fee-for-service (FFS) basis.⁴⁰

The FFS structure is one of two industry standard types of laboratory service agreements that WX offers, the other being the full-time-equivalent (FTE) basis. The FFS agreement is a more flexible project-by-project contract that does not require a long-term commitment. A significant portion of net revenues from these projects—often structured as a fixed price or FFS with a cap—is contingent on successful execution. CROs receive proceeds from the customer during or after the completion of a FFS project.

A FTE arrangement, however, requires the CRO to assign a dedicated team of scientists to the needs of an individual customer for a specified duration. The customer pays a fixed rate regardless of the workload, overtime, or how the assignment may change, and the agreement generally includes material costs. In general, CROs such as WX would hope to start a relationship with a new customer through FFS assignments. If the customer is impressed and satisfied, WX would aim to sign them up for a FTE agreement.

Like most CROs, WX offered very flexible contracts to customers, generally allowing the termination of the agreements or reduction in the scope of services with little to no notice. For the majority of WX's contracts, customers reserved the right to unilaterally terminate the contract upon prior notice ranging from 30 to 90 days. This kind of flexibility made WX an appealing outsourcing partner since it was "cheap to use and easy to dump."⁴¹

In a twist of irony, WX finally won its first FTE contract in March 2003 from Pharmacoepia, providing Pharmacoepia's legacy chemistry business essentially the same service that Li and Baldwin originally proposed to the board. Pharmacoepia's management had wanted to avoid an actual China-based JV but was comfortable in contracting out to

This kind of flexibility made WX an appealing outsourcing partner since it was "cheap to use and easy to dump."

Li's new team. WX agreed to provide Pharmacopeia's clients synthesis of combinatorial chemistry templates, compound libraries, and individual compounds.

"This alliance enables Pharmacopeia to offer the (pharmaceutical) industry timely, high-quality chemistry services and products, with US-based scientific project management at the highly competitive pricing that offshore sourcing provides," claimed Joseph A. Mollica, the chairman and CEO of Pharmacopeia, in a press release.⁴²

In the same press release, Li claimed, "By leveraging Pharmacopeia's synthetic expertise and well-honed client project management skills with WuXi PharmaTech's state-of-the-art offshore synthesis capabilities, I truly believe we offer our mutual clients the best of both worlds."⁴³

The next year, in 2004, Pharmacopeia announced that it would be spinning off its software business as Accelrys. At the time, the discovery chemistry business was more or less breaking even, had been outgrown considerably by the software segment, and anticipated future competition from an expanding array of companies that specialized in this business line.⁴⁴

Not surprisingly, it is difficult for a new startup to be taken seriously by establishment players, such as Pfizer and Merck, for complex outsourcing

projects that involve the exchange of IP. Being the first-of-its-kind China-based discovery chemistry CRO certainly did not make that task any easier. For these reasons, WX needed to establish the company's credibility early on through employee and board relationships and direct work experience with pharmaceutical companies and other potential clients.

Baldwin recalled, "Having several on the board who have broad recognition in the industry is critical for a new company like WuXi."⁴⁵

Daniel Auerbach, a managing director of Fidelity Asia Ventures, one of WX's first institutional investors, agreed. "The experiences and connections of management are phenomenally important. If it weren't for Ge Li, his credibility, and the credibility of the people around him like Dr. Baldwin, he never would have pulled it off. Why? Because they're dealing with IP that's borrowed, worked on, and handed back. If that's ever violated, the company is toast. So having the validation of an incredibly strong international network and the trust associated with that got WX off the ground."⁴⁶

WX's discovery chemistry business grew rapidly, snapping up 12 FTE projects and expanding to 252 employees by the end of 2003.⁴⁷ Since WX's labs were located far from the client, usually in a different country, WX made additional efforts to build trust and rapport.

WX's scientists would convene routine meetings and send daily emails and bi-weekly reports to the chemists at the client companies. The company held English classes for their lab technicians and researchers to improve communications at all levels. An online monitoring and reporting system was also developed to allow a customer's project manager to monitor progress through a secure website.

In addition, to ensure IP protection, WX had put in place an infrastructure— independent labs, IT, and security services—that physically and operationally separated customer projects and could be customized for different client specifications and expectations.



Photo: WuXi AppTec

Move Up the Value Chain or Double Down?

For WX, the discovery chemistry business seemed to be booming as it continued to win assignments and turned out high-quality libraries. The company was accruing valuable experience and credibility and looked to be on a solid growth trajectory. At this point, the startup began contemplating how to evolve the business beyond capturing the cost arbitrage in discovery chemistry.

One area the company explored at this time was moving into the higher value-added aspects of drug discovery. However, conventional wisdom in the pharmaceutical industry deemed it something of a taboo for a service provider to enter into drug discovery because it creates competition for the company's own clients. Furthermore, if the service business is already overstretched, the internal research suffers as capacity is diverted to satisfying the client business. Pharmacoepia had experimented with internal research

to discover and sell molecules at a higher price, but had not been terribly successful in making it work.

To get around these issues, WX considered setting up a separate company in China

that would be wholly owned by WX, Baldwin, and one of Baldwin's former Merck colleagues. The subsidiary would formulate ideas for internal research and then use WX's chemistry outsourcing services to do much of the work. The proposal, however, ran into questions regarding potential legality and logistical challenges and was abandoned thereafter.⁴⁸

Subsequently, Baldwin decided to once again strike out on his own and start a biotech company that would

find promising drug candidates and outsource much of the work to WX. In 2003, he founded Vitae Pharmaceuticals in the United States, a clinical stage biotech company focused on discovering and developing novel, small molecule drugs for diseases, such as diabetes and Alzheimer's, that represent large market opportunities. Vitae became an important early customer for WX, paying anywhere between \$1.2-\$2.8 million between 2004 and 2006 for WX's services.⁴⁹

Rather than pursuing higher value internal discovery, WX decided to double down on outsourcing services by expanding its capabilities to serve more areas of the discovery and development process. The company set its sights on becoming an integrated solutions provider, buttressed by a competitive cost structure. "The consensus was, we will keep putting blocks together until we have a wall," said Baldwin.⁵⁰

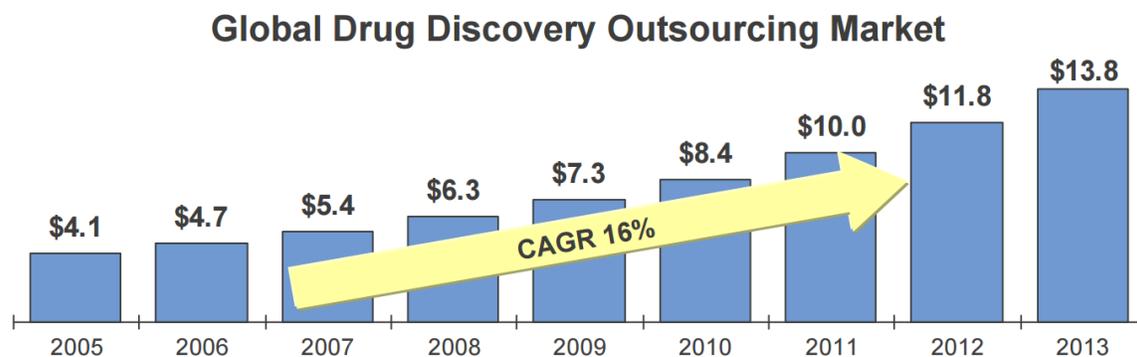
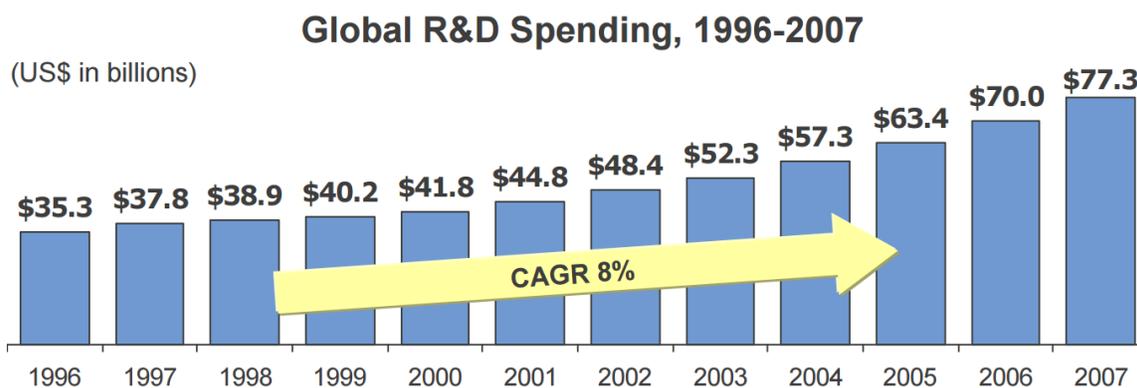
Adapting to Change: Diversification and Expansion

At precisely the moment WX began forming strategic plans to expand services to cover all areas of drug discovery and development, economic pressures intensified on the pharmaceutical industry, creating market opportunities for these services (see Figure 2). Pharmaceutical companies responded by increasing their emphasis on cost control. The market for outsourcing services gradually caught up

to biotech firms in terms of both scale and variety of offerings.

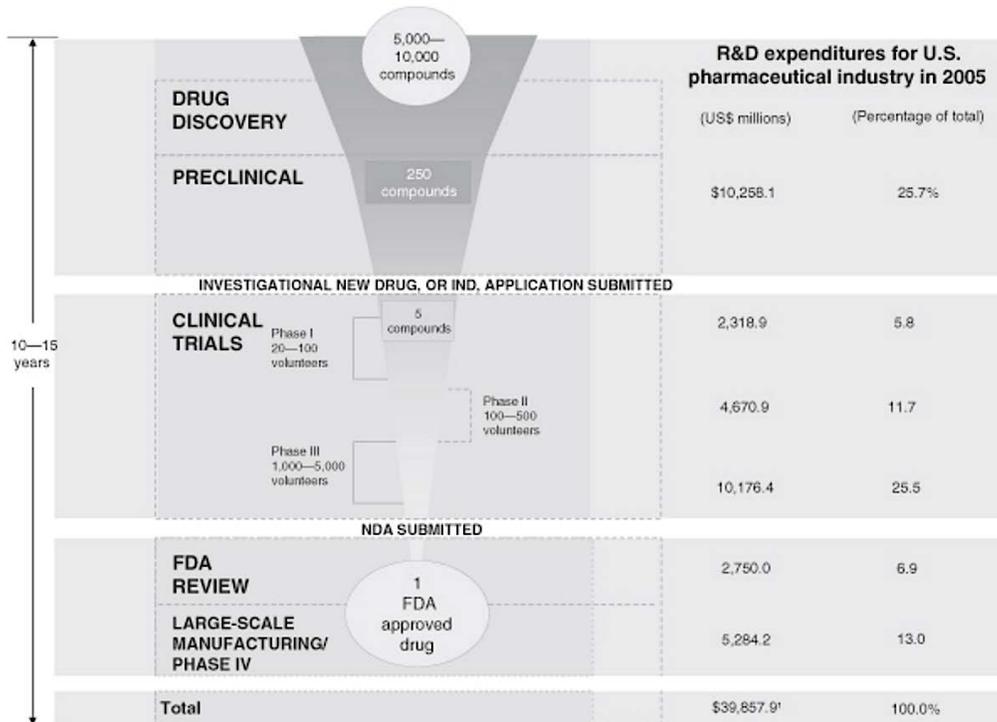
Despite the pressures on the global industry, US pharmaceutical R&D spending was still growing rapidly at around 9 percent a year, from \$20 billion in 1997 to \$40 billion in 2005.⁵² The increased spending reflected the need to plough through mounting difficulties to bring new treatments to patients.

Figure 2. R&D Outsourcing Spending Outgrows Total R&D Spending



Source: Kalorama Information.⁵¹

Figure 3. R&D Spending at Different Stages of the Drug Development Process



Source: WX IPO Prospectus.

Failure rates of potential candidates are very high. For example, for every 5,000 to 10,000 compounds tested as a potential drug, only one will receive regulatory approval and become a new treatment.⁵³

According to *Pharma*, in 2005 it took an average of 10 to 15 years and approximately \$800 million to develop a drug and bring it to market. This includes the capital spent on drug candidates that failed. The cost of developing and bringing to market a biologic drug—one that is produced through a cell culture rather than chemistry—was even higher: roughly \$1.2 billion at 2005 prices.⁵⁴ And even

as these R&D costs were rising, expiring patents, government price controls, and competition from generic substitutes continued to cut into revenues and compress the profit margins of pharmaceutical firms.

Since it can be expensive to hire and maintain specialized teams whose services may no longer be required after a project is completed, pharmaceutical firms could use CROs as effective cost controls for their R&D budgets (see Figure 3). In addition, outsourcing could shorten drug development time by as much as 30 percent, according to a 2004 *Frost & Sullivan* study.⁵⁵

For all these reasons, R&D outsourcing became a common practice. US pharmaceutical companies outsourced just 10 percent of their total R&D spending in 1997, but that rate grew to 24 percent in 2001 and 33 percent in 2005. The proportion of pharmaceutical companies outsourcing at least some R&D activities increased from 37 percent in 1997 to 70 percent by 2005.⁵⁶ Components of early-stage drug development, toxicology, preclinical testing, clinical testing, regulatory approval preparation, and manufacturing were all beginning to be routinely outsourced, particularly for the more “assembly line” testing and labor-intensive activities.

The pharmaceutical sector also followed the biotech industry’s lead in outsourcing primary manufacturing, which includes APIs for approved drugs and chemical intermediates, as well as secondary manufacturing, which involves formulation, dosage form, and packaging manufacturing ranging from small clinical amounts to commercial scale. By the early 2000s, pharmaceutical companies’ demand for outsourced manufacturing was quickly catching up to trends already prevalent in the biotech industry.

Historically, the pharmaceutical industry had been inclined to do its own manufacturing to maximize their return on investment in facilities and capital by operating at full capacity. However, because of the unpredictability of the

drug development pipeline, sizing a plant to maintain maximum capacity can be a challenge. To reduce risks, companies sought to benefit by diverting some of their manufacturing to outsourcing firms, which enabled them to manage unexpected surges in capacity needs without stranding assets during slower periods.

For this reason, in the mid-2000s, the pharmaceutical industry was spending more than \$15 billion yearly on outsourced manufacturing, formulation, and the packaging of drugs, according to a 2006 report by research firm Kalorama Information. It estimated that the market was growing annually at 10 to 12 percent, and that the percentage of pharmaceutical companies that outsourced at least some manufacturing would grow from 35 percent in 2004 to nearly 50 percent by 2009. This study also predicted that the outsourced manufacturing market would exceed \$17.5 billion in 2006 and would reach more than \$26 billion by 2011.⁵⁷

In that kind of growth market, CROs offering a variety of services could capture significant revenue synergies and gain an edge on the competition. Dedicated “procurement groups” in drug companies aimed to match internal research teams’ needs with capable CROs/CMOs. To obtain more favorable pricing from CROs/CMOs, these procurement groups try to bundle services whenever possible. Even putting aside pricing, if a pharmaceutical client is pleased with a CRO’s work on one stage

of the drug discovery pipeline, then they are naturally more likely to use them again for other processes such as preclinical trials, clinical trials, and manufacturing.

Competition Intensifies

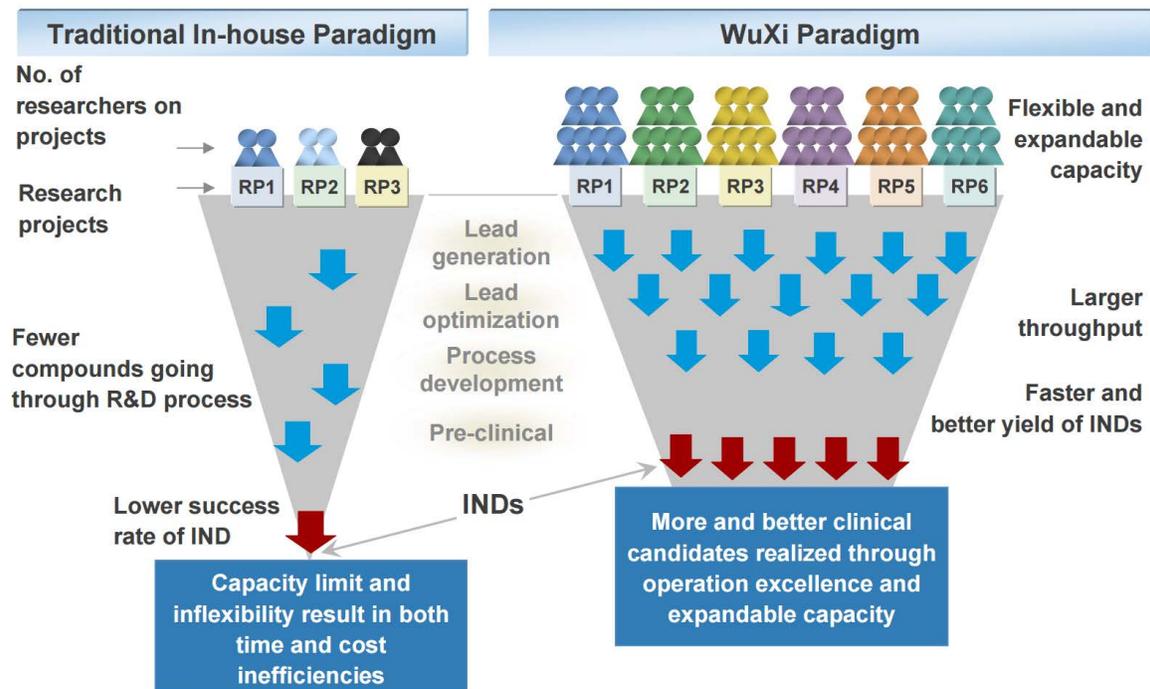
This economy of scale dynamic set off a race within the CRO industry to stay ahead of competitors by expanding service offerings through organic growth and acquisitions.

To illustrate, a typical case of serving a large pharmaceutical company across a range of spectrums could start with a contract to synthesize chemical

compounds (WX’s original services). Then, with leads identified from chemical compounds synthesis, the CRO could develop biological assays for drug screening, which involves the use of live animal or plant (in vivo) or tissue cell (in vitro) to determine the biological activity of a substance like a drug.

The CRO could then be hired to perform the drug metabolism and pharmacopeia kinetics (DMPK) and bioanalytical analysis for elucidation of the compound’s properties. If the compound passed that stage, the CRO could finally be hired to develop the manufacturing process and formulation to produce material for a clinical trial.

Figure 4. Outsourcing Advantages: Greater Flexibility and Capacity



Source: WuXi Pharmatech Investor Presentation.⁶⁰

WX’s strategy to “build a wall” of service offerings reflected this competitive landscape. While a number of US CROs had a head start, the talent arbitrage opportunity in China gave WX a big potential pricing advantage over its American competitors. At the time, the starting salary for a PhD in the United States was roughly \$200,000 a year but just \$23,000 in China, according to research from UBS.⁵⁸ And the supply was abundant as Chinese universities were pumping out more STEM (science, technology, engineering, and math) graduates than their US counterparts.

“I think since day one we realized people are going to be our most valuable asset ... so people ask us how difficult it is to recruit scientists in China,” said Li, “my answer is that it’s not that difficult because China produces 300,000 life science-related raw talent every year.”⁵⁹

By building a wall, WX hoped to evolve beyond a cost arbitrage opportunity into an integrated services and global platform covering small molecules, biologics, and medical devices. WX believed offering broader capabilities, combined with its competitive cost structure, would enhance its value proposition to customers and keep pace with its competition (see Figure 4).

“R&D from WuXi’s point of view is far beyond just the arbitrage of labor

cost,” Li argued in a 2009 speech to investors, clients, and competitors at the annual JP Morgan Healthcare Conference. “We want to continuously build our capability and capacity to provide a fully integrated service to help our partners to improve success of discovery and shorten development time. We believe this is the true value from R&D outsourcing.”⁶¹

By doing so, WX would try to position itself as a “strategic partner” for its clients rather than just an outsourcing service provider. WX would aim to share common goals, engage in joint strategic planning, and experiment with

By building a wall, WX hoped to evolve beyond a cost arbitrage opportunity into an integrated services and global platform.

new business forms with its clients. “The idea was that when X pharmaceutical company lays off

another 5,000 people, WX can go to them and say, ‘look, we have all of these capabilities, give us your business and we’ll do it for you,’” said Baldwin.⁶²

To reinforce the point, Li explained that “WuXi is trying to become strategic partners with a majority of our customers and it’s interesting—because it takes time to gain trust from the customer to become strategic partners. I think the more service capabilities you can offer, the more bonded you are with your customers and the more likely you can have a strategic relationship.”⁶³

WX recognized that the firm needed to move quickly, since it was no longer

the only company of its kind in China. Indeed, WX's success had attracted attention, so new entrants sought to replicate its model. All of a sudden, WX found itself in the position of an incumbent even though it had been a mere startup a few years before.

At this point in the development of the Chinese industry, a number of Chinese returnees, all with extensive experience in the US and European pharmaceutical industries, had also set up discovery chemistry businesses, such as ShanghaiBio, Pharmaron, and Medicilon. These CROs, too, were starting to broaden their service offerings into other areas of drug discovery and development as they tried to ride the industry trend.

At the same time, US CROs were also looking to start new or offshore existing services to China. For example, BioDuro, a CRO based outside of Washington, DC, opened a discovery chemistry laboratory in Beijing with 300 employees.⁶⁴ Indeed, CROs in India were also getting in on the game by expanding their services beyond traditional areas in clinical trials and API manufacturing into discovery chemistry.

In 2003, then, WX established process development services to help customers manufacture their drug candidates more efficiently. For instance, the compounds created for screening in lead generation and lead optimization

are typically synthesized in relatively small, milligram-size quantities. Before a drug candidate can enter preclinical and clinical trials, kilogram-size quantities must be synthesized.

The goal of process development is to improve the ease with which compounds can be synthesized in these larger quantities, typically by minimizing the number of steps, scaling up, and determining how to reduce the time and cost of production.

These services were a natural extension of the early-stage discovery chemistry that opened the door to CMO services, which WX began in 2004. The company had entered the offshore CMO market against well-established rivals in India. To run the business, WX hired a veteran in Indian API manufacturing, Jagdish Sastry, the head of Jubilant Organosys, to develop these manufacturing capabilities.

WX first leased a temporary facility in Taizhou, located in next-door Zhejiang province, and eventually broke ground in 2003 on a permanent 220,000 square-foot manufacturing facility in Jinshan, a Shanghai suburb, with an initial investment of \$7.2 million. In 2004, WX announced plans to invest another \$12 million to expand the facility.⁶⁵

WX obtained a loan from Chinese state banks to finance the construction, and repaid \$4.1 million worth of outstanding debt in 2004. The facility was completed

in May 2004 and WX terminated its lease on the Taizhou facility. Facility utilization remained low for a while as WX's major customers arrived in China to perform audits on whether the facility met strict standards. By 2006, however, these audits were largely completed and WX experienced a surge in manufacturing revenue, dramatically doubling it from the \$24 million in 2005.⁶⁶

Like other CMOs, WX marketed its manufacturing services on a FFS basis. The CMO business has lower gross margins than the laboratory services business and its earnings tend to fluctuate more. This is largely



Photo: Flickr/Novartis

because the shipment of a product is dependent on the customer's R&D progress, which can be unpredictable.

After starting to integrate process research with some manufacturing, WX launched a new vertical in bioanalytical services in 2005, bringing onboard a well-known Princeton University scientist to set up the division. "You have to get the talent before you set up an offering," Baldwin noted. "If someone at the top is recognized, it's much easier to get interest from customers."⁶⁷

Bioanalytical services include quantitative and qualitative sample

analyses to support preclinical and clinical studies of pharmacokinetics, toxicokinetics, pharmacodynamics, and immunogenicity. The services analyze small-molecule drugs using liquid chromatography/mass spectroscopy and measure biomarker/biologics and antibody immunogenicity using immunochemistry. A typical bioanalytical laboratory generates hundreds or even thousands of test

results daily, which must be securely stored for long periods.

Now, having developed a rather mature discovery chemistry business, WX decided to set its sights on biologics. After

clients synthesized compounds with WX, a natural next step would be to hire WX to study their biological properties, such as levels of acidity in a certain in vitro assay, how they perform in vivo, how the drug interacts with the metabolism, where it is stable, and other factors. Furthermore, if these pharmaceutical companies continued to study and tinker with the compounds with a WX biology department, it would reduce the need to ship compounds back and forth from China to the United States, making for a smoother transition.

At the time, in vivo animal studies in the United States were very profitable. A

major cost of such services is obtaining large animal specimens and permitting for DMPK testing. Two of the most widely used large animals for in vivo testing are the cynomolgus monkey and the beagle dog. In the mid-2000s, China was the biggest supplier of cynomolgus monkeys to the United States, and animal testing there did not have the same level of stigma and regulation that existed in the United States and India. This was an additional advantage for WX.

Besides drug testing, biologics were just starting to break out in a big way. Global sales of biologics products reached \$76 billion in 2006, and were projected to double by 2012.⁶⁸ Biological CRO services were also generally much higher margin than chemistry services and required more highly trained researchers to conduct them. Up until then, these areas were the core strengths of US CROs, although several Chinese biologics CROs had already been established.⁶⁹

So WX also began exploring what types of biology services would be profitable in China and decided to start offering DMPK services in 2006. Li had lured Angela Wong, a PhD in pharmacology from Baylor University, back to China in 2005 to head WX's biologics department.⁷⁰

Wong had worked at SmithKline, Pharmacoepia, and Vitae Pharmaceuticals, where she headed a team responsible for selecting CROs

to provide DMPK, PK/PD modeling, animal disease modeling, and toxicology services. (Toxicology involves the scientific analysis of the effects of toxic chemical substances, either in vitro, on cultured bacteria or mammalian cells, or in vivo, in living animals.)

“At that time [2005/2006] we started exploring what type of biologics services would be a profitable business in China,” Wong recalled. “In the middle of the 2000s, in vivo testing was very profitable business for CROs. WX had built an excellent platform with a very large base of collaboration with large US pharmaceutical companies in chemistry. These clients, after they synthesized compounds at WX, would then study their biological properties, either internally or with another CRO. We wanted to capture this business as we knew it could be very profitable.”⁷¹

Establishing biologics would allow WX to capture higher profit margins but it would also be a challenge, as such services require a higher degree of skill. “Because of the nature and variability of the assay, biologics are definitely a more highly skilled service,” Wong said. “Customers need a lot of sorting out and an intensive selection process to pick out a biologics CRO.”⁷²

WX again saw its cost structure as an advantage in this area, particularly for toxicology on large animals. To house the toxicology and DMPK services, WX initially leased and renovated a 13,000

square-foot facility in Xishan, one of six urban districts of Wuxi City and about 60 kilometers from Shanghai.

But with ambitious growth plans in mind, WX decided to instead build a new, state-of-the-art facility for the

business unit. So Wong selected an architect who had designed Merck and AstraZeneca's US toxicology facilities. WX subsequently broke ground on a 215,000 square-foot facility in Suzhou, Jiangsu province, with a goal to begin operations in 2009.⁷³

Financing Growth and Going Public

Although WX invested heavily in new physical infrastructure, CROs generally can monetize their investments in R&D and capital expenditure (capex) much faster than biotech and drug companies. Typically, biotech and pharmaceutical startups are very dependent on VC funding. This is because these companies make R&D investments that most likely will not generate revenue for years, and there is a good chance the investment will never be profitable. By contrast, CROs are paid by the project, so they can partially finance their growth through cash flows and take on more debt in the interim.

The biggest drag on how quickly a CRO can start generating cash from new capex and services

is the wait time for the authorities and customer inspections. Before being chosen for a project, customers usually conduct rigorous due diligence of a CRO/CMO, including on-site audits and referral contacts. Even after signing an agreement, clients still routinely audit and inspect facilities, processes, and practices to ensure that the CRO is meeting both internal standards and complying with regulations in the drug development process.



Photo: Flickr/Kjetil Ree

WX spent the initial equity investments from its founders and Taihushui, proceeds from the land deal, and loans with the help of Taihushui to finance the construction of labs and hire employees. “Ge [Li] didn’t want classic financing (external capital),” Auerbach of Fidelity Asia Ventures recalled, “in line with his very entrepreneurial side, he bootstrapped.”⁷⁴ By 2002, WX had brought in enough clients to operate without any VC money. In fact, the company did not accept any VC

investment in its first four years, except for the initial angel investment from Taihushui.

Taihushui had guaranteed some of the loans and also provided very favorable unsecured, non-interest bearing,

and repayable on-demand loans to WX.⁷⁵ Since WX was paid on a FFS basis, the company generated revenue from the start. The cash flows CROs generate make debt financing feasible, even for a relatively small company. This makes the CRO business model less reliant on outside equity investors than traditional pharmaceutical and biotech firms.

In 2003, the company borrowed \$2.5 million, and then another \$5.3 million in

2004 to finance a new headquarters in the Shanghai Waigaoqiao Free Trade Zone. At the end of 2005, the company’s total debt outstanding was \$14.7 million.⁷⁶

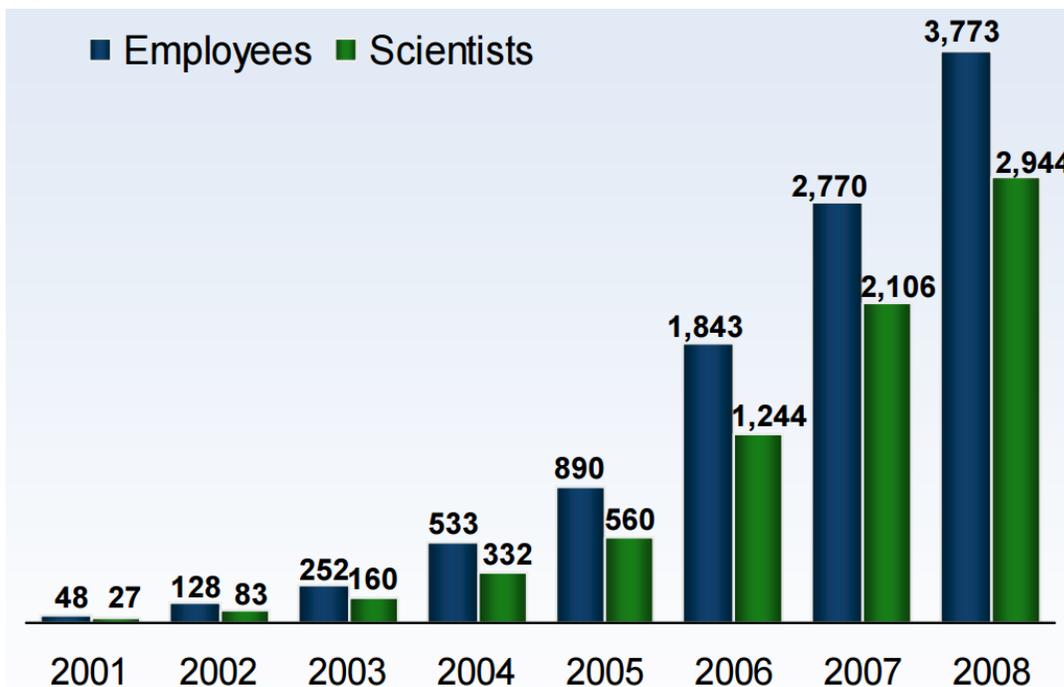
In 2004, WX began negotiating with its initial group of investors to lay the groundwork for a public listing. To gain traction with international investors ahead of an expected initial public offering (IPO), the company decided that it needed to bring in well-known VCs. In addition, its management wanted the VCs to buy out Taihushui, which was a local state-owned enterprise, to avoid the perception of Chinese government control or influence over the company. “We didn’t actually need the [VC]

money,” said Baldwin, “we wanted the recognition.”⁷⁷

So WX brought on an investment banker who had raised money for Pharmacoepia. Given the company’s growth and business plan, WX had little trouble finding institutional investors. WX generated \$20.9 million in revenues in 2004 and was on track to rake in \$34 million in 2005 (see Figure 5).

WX selected Fidelity Asian Ventures and two Singaporean banks, UOB and TianDi Capital, to take a 28.41 percent stake in the company for \$2.21 million. The Fidelity fund had been an early backer of Alibaba starting in 1999

Figure 5. WX’s Rapid Growth Reflected in its Scientist Headcount



Source: WX Investor Presentation.⁷⁸

and was actively investing in China's healthcare sector.

"I first met Drs. Li and Baldwin in 2003," recalled Auerbach. "There were comparable [firms] in the US which hadn't done so well, and there were discussions about a hybrid model that was both a service and product company ... There were a variety of [strategy] iterations between 2003 and 2005, during which I was spending an awful lot of time getting to know Dr. Li personally as a human being but also as an entrepreneur, scientist, and visionary. In the end, the investment thesis was pretty straightforward: it was a labor and quality arbitrage play."⁷⁹

The next year, WX decided it was time to raise money for major capex investments. "Dr. Li decided the time had come to really crank up and do something extraordinary," said Auerbach. In October 2006, WX held a Series B financing round and the same three investors bought in for an additional \$19.2 million. In February 2007, WX brought in more investors for a Series C round during which it raised \$54.5 million. Much of the VC money went into the construction of the Jinshan manufacturing and Suzhou toxicology facilities.⁸⁰

During the first week of July 2007, rumors began swirling in the press that WX was on the verge of an IPO. Later that month, WX completed its IPO filing with the Securities and Exchange

Commission and announced that JP Morgan and Credit Suisse would take WX public on the New York Stock Exchange (NYSE).

During the company's IPO roadshow to investors, WX articulated a vision of building a company that could transform pharmaceutical R&D processes by providing fully integrated services to improve success rates and shorten development time. In particular, WX stressed future growth in the biologics, toxicology, and preclinical testing areas. The firm stated that its objective was to use proceeds from the IPO to invest in expanding its service offerings by growing more organically and exploring strategic acquisitions.

The banks initially proposed pricing WX's shares at \$11-\$13 per American Depositary Share ("ADS," each ADS represented eight ordinary shares). Due to strong demand from investors, the banks raised the price to \$14 per ADS.⁸¹ Consequently, WX raised \$185 million from the offering, of which around \$140 million went to the company and the rest to employees and investors selling shares. The company's stock debuted on the NYSE on August 9, 2007 at \$14 per share.⁸² Existing VC shareholders paid the equivalent of \$2.72 per ADS for their shares; for early investors, a \$14 IPO price represented better than a five-to-one return.⁸³

The stock price doubled in just one month, raising WX's market valuation to \$1.65 billion. It continued to climb from

there, reaching an astounding \$40 per ADS by mid-October. Given that WX's 2006 profits were only \$9 million on \$70 million in revenues, this response suggested investors were very optimistic on the company's growth prospects.

In a short profile of WX in September, *The Economist* seemed to capture the mood: "Even in the overheated world of Chinese IPOs, the listing and subsequent

ballooning of the share in WuXi PharmaTech has drawn gasps ... It would be hard to exaggerate the enthusiasm this suggests."⁸⁴

WX's IPO success certainly got the industry's attention, particularly its chief Chinese rival ShangPharma, which told *Reuters* in October that the company and its private equity backer TPG were also mulling a public listing.⁸⁵

A Good Time to Buy

After WX's highly successful IPO, management now faced the challenge of putting the \$213 million in cash on its balance sheet to work. One of the pitches WX used to woo investors for its listing was that it intended to make strategic acquisitions and partnerships, particularly in areas that would be difficult to build internally.

These plans seemed to comport with general trends in the industry at the time: the CRO industry at this point saw a wave of consolidations in both developed and emerging markets.

A key question would be whether WX might now acquire Chinese and/or Western assets.

After WX's highly successful IPO, management now faced the challenge of putting the \$213 million in cash on its balance sheet to work.

WX's European and American competitors were snapping up existing capacity and building new manufacturing and R&D centers in Asia to keep their pricing competitive against the rapidly growing Chinese and Indian competition, as some of the examples below attest.

Racing To Compete: Acquisitions and Expansions

Swiss CRO/CMO Lonza established API manufacturing in Guangzhou, Guangdong province in 2003. In March 2004, it opened its first R&D

center in Guangzhou, offering process development services.⁸⁶

In 2005, Albany Molecular Research ("AMR"), a chemistry-based drug discovery and development company and one of WX's fiercest competitors in that market, announced it was opening its first R&D lab in India, which broke ground in May 2006 in Hyderabad, India. The new facility raised the company's scientist headcount in India to around 140, with the infrastructure in place to quickly double that number.⁸⁷ In July 2007,

AMR also purchased two pharmaceutical manufacturing sites and additional land for expansion in Aurangabad and

Mumbai to compete with WX's CMO business in API manufacturing.⁸⁸

In June 2007—a couple of months prior to WX's IPO—Connecticut-based CRO Aptuit raised eyebrows when it announced the formation of a JV with a brand new Indian CRO Laurus Labs. Aptuit pledged to pour \$100 million into the project. Commenting on the JV, Michael Griffith, Aptuit's CEO, acknowledged the heat Western-based CROs were feeling from Asian competitors.

"If you look at a list of leading global providers of pharmaceutical services

today, we think that fewer than 20 percent of those companies will be on that list 10 years from now,” he said. “We think that many of the leaders on that list will be replaced with leadership coming out of Asia.”⁸⁹

Conversely, several of WX’s Indian competitors were already making a flurry of acquisitions in the United States and Europe. In 2005 and 2006, Mumbai-based Nicholas Piramal bought UK operations from Avecia and Pfizer. In early 2007, the Indian company announced that it was raising capital to make further US acquisitions, and, according to a spokesperson, “the company is very serious about establishing itself in the US.”⁹⁰

In addition, Dishman Pharmaceuticals, an Indian API manufacturer, in 2006 bought two subsidiaries in the United States and Switzerland of US-based Solutia for \$75 million. Jubilant Organosys, the behemoth Indian CRO/CMO, followed these moves in April 2007 by acquiring Spokane, Washington-based Hollister Laboratories for \$122.5 million.⁹¹

The industry buying spree had multiple rationales: First, to expand service offerings to create integrated platforms for low-cost drug development; second, to level the playing field with Western competitors by buying up US/European operations.

In order to compete globally with the largest US CROs, the Indian firms

believed they needed to transform from regional players to global ones. Moreover, certain activities, such as projects that require close interaction with client scientists and/or involve IP protection issues, are best conducted near the client’s R&D operations, giving international CROs an advantage for certain projects. And in an industry built on trust and reputation, owning US and European operations could enhance credibility with investors, clients, and the general public. The higher level of trust usually leads to more business—a virtuous cycle. In short, proximity was important.

But the Indian firms were hardly the only ones playing the acquisition game. Several of WX’s domestic Chinese competitors, including ShanghaiBio, Bridge Laboratories, and BioDuro either already operated laboratories in the United States or else were setting up sales and marketing operations there. These companies believed that their US presence would allow them to have better and timelier communication with customers, especially the smaller biotech companies.

WX Makes the Move

Within this industry context, on January 4, 2008, WX announced that it had reached an agreement to buy AppTec Laboratory Services, Inc., a US-based biologics and medical device testing CRO/CMO, for \$169 million. In line with the company’s growth strategy, the

AppTec acquisition would immediately give WX capabilities and expertise in biologics testing and manufacturing. In addition, the acquisition would expand WX's US customer base and addressable market, while AppTec would give WX a significant operational footprint in the United States.

"The combination of WuXi PharmaTech and AppTec will bring together complementary service offerings and expertise to create a broad platform covering both chemistry and biologics," Li told analysts at the time. "The combined company will be able to provide more value-added services to our customers in the pharmaceutical, biotechnology, and medical device industries."⁹²



Photo: Flickr/Sanofi Pasteur

AppTec had generated \$71 million in total revenue in 2007. To justify the hefty \$169 million price tag, WX expected AppTec's robust growth to continue. For instance, AppTec's revenue grew 56 percent in 2006 and 38 percent in 2007, and WX expected that mid to high 30 percent growth rate to continue into 2008, with an \$85-\$90 million revenue range for the 11 months of 2008 that WX would own AppTec (the deal closed on January 31). WX expected this revenue growth to be

driven by the opening of an expanded toxicology facility and continued organic growth in biologics testing.⁹³

From Academic to Entrepreneur: Creating AppTec

A detour into the origins of AppTec before WX's acquisition is useful at this point. Among other things, it sets the context for understanding why AppTec became an attractive acquisition target for WX in the first place.

AppTec's history dates to 1982, when Bonnie Baskin founded ViroMed Laboratories. In 2001, Baskin sold three divisions of ViroMed to LabCorp and consolidated

the remaining divisions under a new company, AppTec Laboratories.

Born in Chicago, Baskin followed the example of her scientist and entrepreneurial father Sy Baskin, who ran and owned a successful chemical company. In high school, Baskin thought she had found her calling as a marine biologist after reading Rachel Carson's novel *Silent Spring*, a nonfiction work that documented the harmful environmental and ecological impacts of the widespread use of pesticides. She subsequently enrolled in the University of Miami's marine biology program.

During her first semester in 1966, she had an epiphany during a field trip to Biscayne Bay, an inlet of the Atlantic Ocean on the southeast coast of Florida. She became very seasick and realized that the ocean was not her calling. But she was still interested in pursuing science and ended up settling on microbiology. She went on to earn a doctorate in microbiology from the University of Miami and was awarded a Postdoctoral Fellowship at the National Institute of Health (NIH). Thereafter, she moved to Minneapolis with her then-husband and took a laboratory job working for a professor at the University of Minnesota.⁹⁴

But Baskin discovered that she was ill suited for the life of a university researcher. “I needed to have more people encounters,” she said.⁹⁵ The nature of the work wasn’t the only problem. Now a divorced mother of two boys, Baskin felt the competing pressures of balancing work and family and also that her employer was unsympathetic to the demands on her time.

This was in 1981, when a significant milestone in medicine was about to hit the market. The US Food and Drug Administration (FDA) was on the verge of approving a new drug to treat the symptoms of herpes—the first FDA-approved antiviral drug.⁹⁶

To prescribe the new antiviral drug, Baskin predicted that physicians would need diagnostic testing capabilities.

Prior to that time, clinical virology was primarily done for epidemiological purposes to track outbreaks and for screening at large hospitals that had organ transplant and blood transfusion practices. Most hospital labs did not have the expertise or the required environments for virus diagnostic testing for patients, and there was public concern about contagion.

Baskin decided that the time was right to open a new kind of private clinical virology laboratory to do diagnostic testing for physicians and hospitals. “Without any business experience and not much of a business plan to speak of, I began doing some back-of-the-envelope calculations on how I could make this work,” Baskin recalled.⁹⁷

In an effort to differentiate her new venture and garner attention, she settled on the idea of a “lab on wheels”—retrofitting and remodeling a van into a mobile lab with an incubator that could keep the viruses alive until they could be processed in a permanent lab.

Not only was Baskin’s idea catchy, it also addressed a practical concern that nearly every potential customer would have: how to get the samples from hospitals into the lab before the viruses die. Since viruses need a host to survive, they tend to not live long once they are outside the body. So it is not unusual for a diagnostic test to return a false negative result if the virus dies before testing begins.

The solution is to pick up the samples at hospitals and immediately put them in the incubator with special food in the back of the mobile lab. The van would then return to a base lab at the end of the day and fully process the samples.

Baskin began floating her business proposal with various hospitals and universities around Minnesota, inquiring whether they would send samples, and, if so, approximately how many. “It (the plan) was well received because it gave the physician the opportunity for much better results,” she said.⁹⁸

After Baskin convinced two colleagues at the University of Minnesota to join her, she established ViroMed in February 1982 with the lab on wheels and a main lab located in an 800 square-foot basement.

Business picked up quickly, validating Baskin’s hunch that doctors would start testing for herpes and other viruses as the new drug came to market. Her timing proved fortuitous in other ways as well.

That year, *Newsweek* and *Time* both ran stories about the STD epidemic on their magazine covers, with *Time*’s provocative cover featuring a couple uneasily staring at each other over a skin-colored background and a screaming, bright red headline: “*HERPES, Today’s Scarlet Letter.*” Soon after, the HIV/AIDS epidemic began

sweeping the United States, further raising the demand for ViroMed’s clinical diagnostic services.⁹⁹

Faced with some early challenges, the company was able to turn them into opportunities for expansion into complementary lines of business. One of those challenges involved obtaining the cell cultures needed for viral diagnostics testing. At the time, two east coast companies were the only suppliers of the cell cultures ViroMed needed, and their minimum order quantities were too large for a startup with very little volume. Buying high volumes was also

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very wasteful as cell cultures have a short shelf life of only about a week, so unused cultures had to be thrown away. “That

would bring up my cost of doing the test to a prohibitive point,” Baskin recalled. “It was a real dilemma for me.”¹⁰⁰

But Baskin had learned how to create cell cultures during her graduate work, so she decided ViroMed would start producing its own cells rather than rely on suppliers. She reached out to another lab startup in the twin city of St. Paul that she suspected must be facing the same problem. She proposed that ViroMed would buy an initial cells batch from suppliers on the East Coast, reproduce them, prepare them, and sell the other startup what it needed and keep the rest. The two companies quickly struck a deal.

So Baskin proceeded to buy an original stock of cells from the Federal Depository, and contracted with primate centers to obtain monkey kidneys on a weekly basis to begin producing cell cultures for viral diagnostics. Soon, ViroMed began making all the cells the other lab needed, not just the monkey kidney cells. It didn't take long for ViroMed to scale its cell culture business and broaden its customer base to include big players like the Mayo Clinic.

Another challenge was dealing with the harsh Minnesota winters that impeded the company's new product line. The cell cultures ViroMed shipped would often freeze, thus killing all the cells and destroying the product. But then an innovative solution struck Baskin on a Colorado ski trip when she noticed the exothermic hand and foot warmer packs for sale in the ski shop. "It occurred to me: why can't we use these to put into boxes with cell cultures to keep them from freezing?"¹⁰¹

After a botched attempt that fried the cell cultures, the exothermic ski hand and foot warmers worked. The stopgap solution was enough to keep shipping cultures throughout the winter to buy the company time until it developed special foam containers. Before long, the startup grew into the largest cell culture business in the United States, selling about 150,000 units per week without mandating prohibitively high minimum orders.¹⁰² The two East Coast-based suppliers eventually went out of business.

Diversifying Business Lines

In the early 1990s, with the clinical virology and cell culture business firmly established, Baskin looked for new growth toward the testing portion of the CRO industry. "We had a broad expertise in microbiology, and we asked ourselves, how can we diversify and still utilize our core expertise?" she recounted. "We were in Minneapolis, a 'la-la land' of medical device companies. The industry is highly regulated—the FDA requires a ton of testing—there's high barrier to entry, and we knew how to do it."¹⁰³

ViroMed opened a division for the tissue bank industry for heart valves and for screening human cells, tissues, and cellular- and tissue-based products. The company was also successful in this particular area, becoming the largest tester for the tissue bank industry in the United States, providing comprehensive laboratory services to meet the unique testing needs of the tissue and eye bank industry.

In the process, Baskin met a woman who owned a medical device testing company in Atlanta, Georgia. The entrepreneur was a nationally recognized expert in a type of medical device testing, and the two women clicked. They soon agreed to a deal that saw ViroMed buy and run the Atlanta company, which had about 25-30 employees.

In 1997, ViroMed learned of an opportunity to purchase Quality Biotech, a New Jersey-based lab that specialized

in the testing of new medicines. The company specialized in virology testing strictly for pharmaceutical companies, but was encountering serious problems with testing for a hepatitis product, raising the specter of significant liability and spooking its VC investors.

During the due diligence process, Baskin concluded that the VCs' fears were not warranted and that the fire-sale price was actually an attractive opportunity.

The deal closed for a very low price, beginning a long and painful but ultimately successful integration.

“It wasn’t the liability with the testing that justified the cheap price,” Baskin reflected, “but the company itself was so poorly run, and there were significant cultural differences between our teams. While it only cost us pennies on the dollar to buy, it cost us over a penny to get it working.”¹⁰⁴

It was during this period the idea of forming ViroMed’s own industrial group began to germinate—it would offer a spectrum of testing services for both medical device and biologic therapeutics serving medical device, biotech, and pharmaceutical companies. Prior to this time, the outsourcing for device testing and R&D was stove piped—some labs did testing for the device industry,

others for pharmaceutical companies, and others for biotech, without much overlap.

“I didn’t think it should be siloed,” Baskin said. “The industry is a continuum: device, biologics, and pharma flow together, so why not create a company that has bigger scope and bring together the different customer bases?”¹⁰⁵



Photo: Flickr/S2N82

As the stock market boomed in the late 1990s, the high valuations of publicly traded clinical labs caught Baskin’s attention. In the fall of 2000, she attended a healthcare conference that featured the CEO

of Laboratory Corporation of America (LabCorp). Historically, ViroMed had not competed with LabCorp, since the former specialized in small-scale esoteric testing, while the latter focused on massive fixed-price contracts for more standardized testing. LabCorp in 2000 generated revenues of \$1.9 billion and employed nearly 19,000 people worldwide.¹⁰⁶

During his speech, the LabCorp CEO emphasized that esoteric testing was the future of the company because of the niche’s higher margins and progress in discovering treatments for various

ailments. “Listening to his talk made me concerned,” Baskin recalled. “If LabCorp decided to enter the market, how would we compete?”¹⁰⁷

In the face of this potential threat, Baskin decided that her best move would be to sell the clinical diagnostics division of ViroMed, which pulled in \$26 million in revenue in 2000, to LabCorp or another buyer. She proceeded to contact a healthcare investment banker at Piper Jaffray & Co. to begin exploring a deal possibility. In May 2001, LabCorp purchased ViroMed’s diagnostics testing division, clinical trials division for pharmaceuticals, and cell culture division for around \$40 million.¹⁰⁸

AppTec Is Born

Baskin kept the new industrial part of the company, which included the biologics and medical device testing units, because these were just starting out and had yet to turn a profit. She renamed the entity “AppTec Laboratory Services,” launching the new firm with 130 of the 350 employees that had been at ViroMed and \$12 million in revenue at an operating loss.¹⁰⁹ Baskin set a strategy for the company as a CRO/CMO that served biotech, pharmaceutical, and medical device customers.

To expand the company, Baskin wanted to establish a biologics manufacturing business. The most commercially successful biologics, or what Baskin calls “the blockbuster of biologics,” were a

class called “monoclonal antibodies” that have a wide range of applications.

Monoclonal (meaning all of one type) antibodies are clones of a single parent cell, which basically means there are many copies of a specific type of antibody that recognizes and attaches to a specific protein. They are used to treat diseases like cancer, Crohn’s disease, and arthritis, and are also used in diagnostic tests. Doing this kind of biologics manufacturing also had the potential to establish a project pipeline into AppTec’s biologics testing business.

Baskin had ambitions to build a company significantly larger than ViroMed but recognized that substantial capital would have to be raised for a new facility to manufacture biologics. A new facility would allow AppTec to move from only providing laboratory testing for medical device, bio-pharmaceutical, and biotech firms to also providing manufacturing services for businesses with products moving into clinical trials. In addition, all the employees and services at a Camden, New Jersey facility (formerly Quality Biotech Inc.) would be likely relocated to Philadelphia, Pennsylvania—the intended site of the new facility.

Why Philadelphia? For one thing, the Mid-Atlantic region of the United States is a hub for pharmaceutical and biotech companies. And Philadelphia’s municipal government offered a generous package: tax incentives, no sales tax, grants, and low-interest loans. Stauback

Co., a national real estate firm founded by former Dallas Cowboys quarterback Roger Staubach, helped AppTec evaluate 20 potential sites in the city.

The company settled on a site in the 195-year-old Philadelphia Naval Shipyard, which had 11,000 employees before the Navy shut it down between 1991-1995. In 2000, the city government took over the shipyard to begin redevelopment, designating it a “Keystone Opportunity Improvement Zone.” Businesses that located there would be exempt from state and local business and property taxes until 2015.¹¹⁰

Despite the fact that 2002 was not an ideal time to raise money, since it coincided with the trough of the dot-com bubble bursting, Baskin still found VC investors—Brightstone Capital, Minnesota-based Affinity Capital Management, and Thomas McNearly & Partners, who together invested \$14 million.¹¹¹

“AppTec was an appealing investment, because Bonnie had a prior track record of building and exiting a business,” David Dalvey, a partner at Brightstone Capital, told *Upsize Magazine*. “As a venture capitalist—if I’m doing my job—90 percent of my due diligence and final decision is made on the people. AppTec was an existing business with revenue and some history. Also important,

Bonnie understands the industry, has good industry contacts, and a good reputation.”¹¹²

Dalvey also noted the good exit opportunity for the investment given the consolidation trend in the CRO/CMO industry. “Several large conglomerates nationwide are buying companies like AppTec, and if Bonnie decides to sell, she could sell for an attractive multiple,” he said in March 2004. Ed Spencer, Affinity Capital chairman and founder agreed: “AppTec had a good core business that was generating revenue. More importantly, the company was moving into new businesses that had significant growth potential. With startups, it’s usually the latter. Not both.”¹¹³

AppTec used the new capital, along with a \$3.7 million loan of federal military base closure funds from Philadelphia Industrial Development Corporation and a \$500,000 loan and \$250,000 grant from the state, to build a \$28 million, 75,000 square-foot facility. As discussed above, this was around the time that pharmaceutical companies began to focus on sales and marketing, while outsourcing R&D, clinical testing, and manufacturing services to CROs, so the market seemed ripe. Of the 200 employees hired during the first phase of the project, 75 percent held doctorates.¹¹⁴

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Several facilities now enabled the company to expand its services from traditional biologics and medical devices to newer cell therapeutics and biologics-based devices: the new Philadelphia facility; AppTec's 63,000 square-foot St. Paul facility for in vitro and in vivo biocompatibility, small animal toxicology, contract cGMP manufacturing and processing for tissue-based products; and its 46,000 square-foot facility for microbiology, medical device chemistry, sterilization validations, and package testing in Atlanta.

After the Philadelphia facility began operating in 2004, revenue rose

rapidly from \$22.8 million to \$71 million in 2007—a 46 percent CAGR. In that same year, biologic testing accounted for 69 percent of AppTec's revenue, and manufacturing made up the rest. Nearly two-thirds of AppTec's customers were in the bio-pharma industry, and 37 percent were in the medical device industry. AppTec had built out a broad customer base of 700 companies, ranging from large pharmaceutical companies to small biotech startups. And it employed 495 professionals across three FDA-registered facilities totaling 176,000 square feet.¹¹⁵

The WX Connection

In the spring of 2007, Baskin decided it was time to exit again by selling her company. “We had a sexy company, really starting to hit its stride,” she recounted. “I had no desire to become a public CEO ... It didn’t look like a lot of fun to me.”¹¹⁶ Moreover, Baskin had also started a horse racing business with her father that she hoped to spend more time pursuing. She again called the investment bankers at Piper Jaffray to look for a buyer, and this did not prove particularly difficult as buyers from Europe to Asia soon courted the company.¹¹⁷

Buyer Found

“We heard about this company, WuXi PharmaTech, that JP Morgan was taking public. It was a Wall Street darling at the time of the IPO. We all thought it would be an interesting company because they were looking to be global and have a presence in the USA,” Baskin said, “I think they were particularly interested in the Philadelphia site, because that’s where much of their customer base was.”¹¹⁸

“I had some concerns, particularly regarding the common perception that women are not given the same opportunities that men are given in many Asian companies,” she continued, “and they seemed to have a little

different business philosophy, with a hard driving entrepreneurial culture. But it was time to sell. I thought they were really smart, and I was impressed by their US training. Dr. Li struck me as a very smart, savvy guy, and he showed a lot of respect for the business we had built.”¹¹⁹ The two sides subsequently entered a long due diligence process, and ultimately closed the deal in January 2008 without noticeable hiccups or concerns.

“...But it was time to sell. I thought they were really smart, and I was impressed by their US training. Dr. Li struck me as a very smart, savvy guy, and he showed a lot of respect for the business we had built.”

With AppTec now under the wings of WX, the Chinese firm chose not to separate its operations into geographic regions. Instead, WX settled on

splitting the company into two divisions: laboratory testing and manufacturing. Management justified this decision based on the fact that much of WX’s China-based operations’ sales, general, and administrative expenses (SG&A) came from the United States, such as its US-based sales force and marketing expenses.

Its traditional chemistry-based services would remain in China, and WX would integrate AppTec’s toxicology and biological testing services into this division. These US operations focused on AppTec’s existing small animal toxicology, commercial lot release testing, medical device testing, and viral

clearance services. WX management said it intended to “amplify” these services in China rather than completely transferring them overseas. The manufacturing division would include the API manufacturing in China and the biologics manufacturing in Philadelphia, where WX intended this business unit to remain into the foreseeable future.

Exploiting Complementarities and Boosting Opportunities

Unlike WX, which primarily served a smaller number of large pharmaceutical companies, AppTec primarily served a larger number of small to medium-size biotech and medical devices companies. AppTec already had over 700 clients in total and about 20 manufacturing clients,¹²⁰ making its revenue base more diffuse than that of WX.

For instance, AppTec’s top 20 customers accounted for 50 percent of its total revenues, while WX’s top ten customers accounted for approximately 70 percent of the company’s revenues (WX had just 70 customers in 2007 before its acquisition of AppTec).¹²¹

Therefore, the merger would diversify and grow WX’s customer base both by sheer number and into different types of companies. Having relied heavily on large pharmaceutical customers before the acquisition, the loss of a single client would have dealt a great blow to WX. That meant these types of clients had very strong bargaining power during

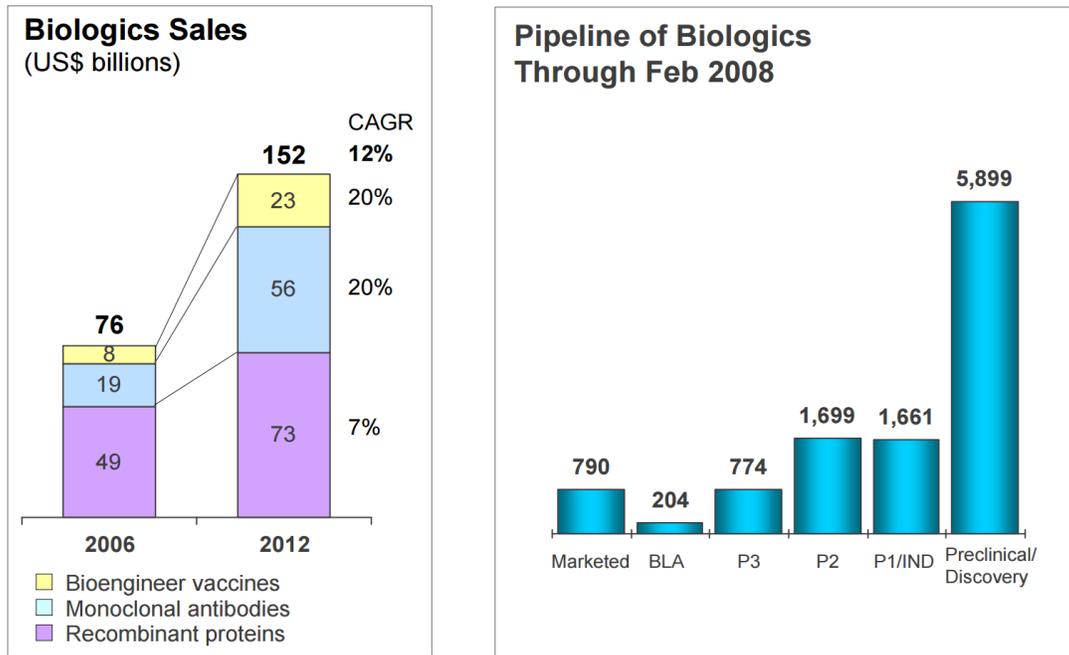
contract negotiations. Such customer diversification, WX believed, would reduce its overall risk profile.

While WX had started developing biologics testing and toxicology services in China, WX and AppTec’s service offerings and customer bases did not really overlap. Edward Hu, WX’s CFO, told investors, “The companies’ [WX and AppTec] are so complementary—there really is no overlap per se, therefore we intend to keep the operations in the US almost as is as we integrate.”¹²²

In an interview, Baldwin further elaborated on the complementarity between the two: “You accomplish two things here. First, you accomplish a US presence for the company. Now you have a Chinese company with a sizable US company underneath its wing. And so it gave a lot of credibility to the [Chinese] company. Second, it gave them a group of specialists to work in the analytics of large molecules. It was all kind of diagnostic stuff they were doing, so they got a foot into a whole new phase of drug therapy that was evolving. And that’s not easy to develop as a priority. I think it was a smart move, whether it was economically smart, I don’t know, but certainly it gave credibility to the company.”¹²³

WX’s management said that they prized AppTec’s biologics manufacturing capabilities above all, because they believed it had the potential to be a lucrative business but one that would

Figure 6. Expectation of Robust Growth in Biologics



Source: 2008 WX Investor Presentation.¹²⁵

have been difficult to develop internally (see Figure 6).

“The decision [to buy] AppTec is complex and there were several important reasons. One of the major reasons was that WX saw the potential of the fermentation of the biologics manufacturing protein-related drugs like antibodies,” Wong said. “In the late 2000s, it wasn’t a good time to start that business in China because there wasn’t the talent pool there to develop it.”¹²⁴

Biopharma manufacturing in the Philadelphia facility generated around \$22 million in revenue in 2007, representing 31 percent of AppTec’s total revenue. For AppTec, this biologics

manufacturing business also served as a pipeline into the facility’s testing business, which generated around \$13 million in revenue in 2007. The Philadelphia facility’s combined operations accounted for about half of AppTec’s total 2007 revenue.

And yet the facility’s utilization for biopharma manufacturing had been pretty low over its first few years of operation—historically around 40-50 percent.¹²⁶ WX became aware of the low utilization rate for the biopharma manufacturing during its long due diligence process before buying the company.¹²⁷ Because of the highly talented workforce and sophistication of the facility, the biopharma

manufacturing business had high fixed costs—over \$10 million a year on about \$22 million in revenue in 2007.¹²⁸

Given the expected growth in biologics, WX believed that a stronger biopharma manufacturing project pipeline would materialize from small biotech clients that AppTec had traditionally served. Just as important, WX was confident that it could convince the company's large pharmaceutical clients, which still did their own biopharma manufacturing, to begin outsourcing this function.

Both of these factors—stronger demand from biotech firms, and opening up a new area of pharmaceutical outsourcing—would solve AppTec's biopharma manufacturing underutilization issue and grow the revenue of the Philadelphia facility.

WX planned for the biologics manufacturing division to build up a solid and steady customer base until the Philadelphia facility was at full capacity. Then, any additional capacity expansion would be transferred to its China operations based on the US knowledge transfer.

"Historically, AppTec focused on the biopharma's business development with small biotech companies," Hu told investors. "Going forward, by leveraging WuXi's relationship with big pharma, we are working on establishing long-term collaborations with big pharma customers to provide integrated cell

line, process development and early-stage clinical manufacturing services, including a full spectrum of biosafety testing services."¹²⁹

AppTec had a small toxicology business in Minneapolis that focused on three types of services: protein molecules (biologics), medical devices (biologics), and small molecules (chemistry), each accounting for about a third of the business.

In this area, WX also saw the opportunity to cross-sell AppTec's small-molecule toxicology business to WX's existing customer base. While WX's own toxicology facility was under construction in Suzhou, that facility, when completed, would primarily focus on testing on primates and other large animals. AppTec's toxicology services, however, mostly used smaller animals like mice and rats, so it made economic sense to keep these services in the United States.

In June 2008, WX announced that it had agreed to a framework agreement to form a 50-50 JV with Covance, the largest CRO in the world, to offer preclinical large animal toxicology services. WX's offer in the partnership included the soon-to-be-completed Suzhou facility and the facility's workforce. Covance would, in turn, contribute \$30 million and the operational and procedural know-how to get the facility up and running quickly. This would allow WX to get revenue flowing into its new facility faster than it would be able to do on its own.¹³⁰

However, shortly thereafter, WX announced that the JV agreement had fallen apart. Company representatives told analysts and investors that without Covance's expertise, it would now have to rely heavily on WX's new AppTec toxicology colleagues to get the facility up and running.

"We know this is going to be a huge challenge," Li said on a conference call. "We never underestimated that [in the decision to terminate the JV]—it's just a huge challenge. But we're going to highly leverage our US operation."¹³¹ WX subsequently moved its senior toxicology director from Minneapolis to Suzhou for many months and began an exchange program of technicians and scientists between the two facilities.

"At that time, there were a lot of exchanges of scientists between AppTec in the USA and us in China, especially in toxicology. We shared our SOPs (standard operating procedures) and also assay protocols. At the beginning, it was quite beneficial," Wong reflected. "AppTec scientists came to help establish quality systems. We made sure both sites [were] using the same quality control systems and replicated a lot of their procedures in China."¹³² This cross-border collaboration would prove crucial to opening and scaling up the Suzhou facility on time.

WX was not immune to these effects of the financial crisis, which created enormous difficulties as it sought to successfully integrate with its new AppTec acquisition.

Plans Derailed

In the second half of 2007, however, a funding slowdown started to hit the biotech industry, and AppTec continued to have problems with utilization of its biologics manufacturing facility. Full capacity utilization for AppTec's biologics manufacturing was only around five manufacturing projects at once, so the cancelation of just one project would cause a significant drop in capacity. Still, WX hoped to cross sell its manufacturing services to large pharmaceutical clients who would agree to more stable contracts over longer periods to sustain operations at full capacity.

But as 2008 progressed, ripples from the global financial crisis took a huge toll on small and medium-size biotech companies. Even larger firms felt the pinch of what became a severe global recession. By the end of 2008, more than 40 percent of small biotech firms had less than one year of cash remaining, and over 30 percent of small, publicly traded firms had less than six months of cash to survive.¹³³ As a result, these companies began hoarding cash and cutting back on R&D, which meant less outsourcing.

This trend would continue for several years. From 2008 to 2011, a quarter of all publicly traded biotech firms were either acquired or shut down completely.¹³⁴ Further, in response to

the financial crisis, many of WX's large pharmaceutical clients undertook efforts to review and then restructure their own operations.

WX was not immune to these effects of the financial crisis, which created enormous difficulties as it sought to successfully integrate with its new AppTec acquisition. First, many of AppTec's established clients were in severe financial straits, especially in the biologics manufacturing space. This caused the Philadelphia facility's biopharma manufacturing utilization rate to drop even lower.

While the testing component of AppTec and WX businesses were more stable as clients still needed to keep testing for safety and effectiveness of new products, manufacturing projects have a much longer time horizon and are harder to commit to during periods of vast uncertainty.

In the company's first quarter 2008 conference call with investors, WX disclosed that AppTec's biologics manufacturing had fallen behind the revenue target set at the start of the year. Two stalled projects, one resulting from a cell line quality issue and the other due to failure of a clinical trial candidate, were blamed for the setback. Nevertheless, WX's management reaffirmed their revenue guidance from the beginning of the year, arguing that they expected to see an increase in the utilization rate.

Yet WX had more bad news to tell investors during the second quarter conference call that summer. Management disclosed that the biologics manufacturing business had experienced further project cancellations and could not win a sufficient number of new projects to offset lost business.

WX's pharmaceutical clients' own restructuring efforts also hindered the company's effort to cross-sell biologics manufacturing to them. These companies had their own biologics manufacturing capabilities, and WX had hoped that by adding the service, they could convince large pharmaceutical clients to outsource these services to WX instead.

But it turned out that these companies' internal review processes were delaying decisions on whether to rely on outsourcing biologics manufacturing. In spite of these headwinds, WX maintained its revenue guidance for 2008, saying that it expected AppTec's business to pick up in the latter half of the year.

By September, Lehman Brothers had filed for bankruptcy amid turmoil in the financial markets, and in the following month, WX finally cut its revenue guidance for 2008 by \$15 million to \$40 million. The shortfall was on account of the biologics manufacturing business and the knock-on effects on biologics testing related to manufacturing projects that have significant testing requirements.¹³⁵ WX management

also discussed inquiries from clients requesting that WX move biologics manufacturing to China to facilitate more cost savings that would help weather the economic downturn.

“Due to cancellations and the delays from our small biotech clients, our biologics business is not performing as well as we expected,” Li explained on a conference call announcing the adjusted guidance. “[The] shortfall is really coming from the funding environment. We anticipated more projects to be signed up by now, but those customers have been delaying their decision now. And the ones who have already signed up, they’ve basically cancelled or delayed. Everybody is trying to save money at the moment.”¹³⁶



Photo: WuXi AppTec

WX’s management did, however, reaffirm the strategic rationale for the AppTec acquisition, expressing confidence that the biologics manufacturing business would pick up once macroeconomic conditions improved.

Hu, who has changed jobs from CFO to COO of WX as of this writing, described the biologics manufacturing situation this way: “We’ve been hit by a perfect storm. Earlier in the year, we had a cancellation because of a company

product’s clinical failure ... several projects cancelled that way. And then the second wave of delays were due to cell line issues. And then lately, we see the postponement and cancellation is mostly due to funding issues.”¹³⁷

The next month, on WX’s third quarter earnings call, management disclosed that its biologics manufacturing utilization had continued to deteriorate and a turnaround in the fourth quarter was not expected.

WX’s management told analysts and investors they were looking into “strategic options and alternatives” for the Philadelphia facility since the challenge that business line faced would endure. Due to the restructuring exercises underway at many of WX’s pharmaceutical clients, WX explained that it was not having success replacing the lost business and customers.

On December 2, 2008, WX announced that it would be shutting down its biologics manufacturing operations in Philadelphia. Given the high fixed cost of this business line, WX decided that waiting for an economic rebound would be too much of a drag on the entire company.

“When we made the [AppTec] acquisition decision, we held the belief that biologics capability is an essential

part of our future growth strategy. When we did the deal, that thesis was pretty strong,” Hu explained on the investor conference call. “And then over the last three to six months, the economic environment deteriorated significantly, and impacted the business by constraining biotech companies’ ability to finance those early-stage manufacturing projects. And therefore we don’t see a turnaround in the foreseeable future.”¹³⁸

Biologics manufacturing capability was precisely the segment WX most coveted at the time of its AppTec acquisition. And so the speed at which that segment collapsed is notable. Ultimately, WX would lay off around 100 of AppTec’s 490 employees through workforce reduction and employee attrition. With the closure, WX had to write down \$60.5 million on its AppTec acquisition.¹³⁹ (In the next quarter, WX increased this write-down

to \$110 million, a huge sum considering it had paid \$169 million for AppTec just a year earlier.)

“In retrospect, we wish we had foreseen the unprecedented economic downturn and credit freeze that severely impacted many of AppTec’s customers,” Li told investors.¹⁴⁰ After this December 5 conference call, WX saw its stock price plummet to a staggeringly low \$5 per share.

A J.P. Morgan analyst also proffered his view on the buyout, “The 2008 AppTec acquisition in hindsight was more of a disruption than an enhancement. Although the strategic rationale for buying AppTec remains in question, the decision to exit US biologic manufacturing should drive cost savings this year as WuXi will now shift the US focus to existing capabilities, including biologic testing, cell banking, and therapy services.”¹⁴¹

Conclusion

WX's acquisition of AppTec was a disappointment but not a complete disaster. The timing of the deal could not have been worse. While potential signs of trouble ahead were evident around the time the deal closed, such as the low utilization rate of the facility and growing indicators of an economic shock, it is hard to fault WX's management for not anticipating the global financial crisis and its subsequent impact on the biotech and pharmaceutical industries.

Biologics overall were beginning to break out in a big way. To stay competitive, WX recognized that it needed to quickly develop a strong biologics outsourcing segment as part of a fully integrated platform to offer its clients. And to keep up with the rapidly evolving CRO business, WX knew that it had to extend itself beyond its legacy chemistry outsourcing and manufacturing offerings.

Viewed in this light, WX's strategy to pursue acquisitions and JV partnerships to ramp up those new service offerings was, in many ways, based on a proper diagnosis of the market dynamics and competitive landscape at the time.



Photo: WuXi AppTec

WX intended for the AppTec acquisition to jumpstart its push into biologics outsourcing, which required highly skilled and technical talent that was not available in China. It could have been a differentiator for WX since few CROs at the time offered such services. With a technically oriented US company under its wing, such an acquisition could also change the perception of WX from a low-cost, regional outsourcing provider

to a global CRO competitor on par with leading firms in the industry.

WX clearly failed to execute its plan to ramp up biologics manufacturing in Philadelphia. Yet the company's integration efforts

with biologics and medical device testing were much more successful.

For instance, WX successfully integrated AppTec's legacy toxicology business and leveraged it to quickly monetize WX's Suzhou toxicology facility. Such an effort became even more crucial after the Covance JV deal collapsed. Moreover, WX's US-based testing business has continued to grow since the acquisition, and is substantially larger today than it was in 2007.

As is the case with many cross-border acquisitions, analysts raised concerns at the time about whether WX would be able to retain AppTec's key employees. And since relationships are so vital to the CRO business, it was widely presumed that a large part of the deal's success hinged on the extent to which WX would be able to retain key management and scientific personnel at AppTec.

Analysts also questioned whether AppTec's employees feared the potential for WX to "cut and paste" AppTec's services from the United States to China, and whether such a concern would trigger a mass exodus of employees from the company.

Those concerns ultimately did not materialize as WX demonstrated its commitment to the US operations and was relatively successful in retaining AppTec's key personnel.¹⁴² Nor did problems in the aftermath of the deal scare WX away from making additional acquisitions of US-based businesses. In fact, it has made several more since 2008.¹⁴³

On a broader level, then, WX's experience reflects the rapid emergence and evolution of the global pharmaceutical R&D industry. Faced with economic pressures and the impetus to change over the last 15-20 years, pharmaceutical companies had to adapt to new business models, including those that led to the emergence of the CRO/CMO industry. India and China have been

able to capture this outsourcing bonanza by building out their own companies and capabilities.

As China and India continue to attract talented returnees into their respective domestic biotech and healthcare sectors, similar acquisitions of US CROs may become less common. In addition, improved technology and communication has lessened the perception that geographic proximity is important to build and maintain relationships with clients.

Offshoring of healthcare and biotech research jobs to China and India will probably continue for some time, although it will likely slow as the labor cost differential converges and as homegrown human capital makes talent arbitrage opportunities less appealing.

Much of this anticipated future depends, of course, on whether China can successfully develop a domestic healthcare and biotechnology industry, replicating its success in the CRO sector. Such an endeavor will likely require the similar network of Chinese "returnees" that proved so central to the development of China's CRO/CMO industry. One potential risk in the near term, then, may be that a seemingly harsher political environment in China could deter overseas Chinese students and talent from returning.¹⁴⁴

Another challenge is that China will have to continue competing with India

to develop these industries as it did in the CRO/CMO realm. With its own large and talented diaspora and a low-cost business environment, India possesses many of the same advantages as China for these services.

In the near term, the CRO/CMO business will continue to grow, but the industry's long-term prospects surely depend on what happens in the pharmaceutical and biotechnology industries more broadly.

Although 2014 proved to be a banner year for drug discovery, with the US FDA announcing a total of 41 NCE approvals for treatments, the prior 10-year average was just 24 per year.¹⁴⁵ Moreover, most of the approvals were actually for niche drugs. For instance, of the 100 top selling pharmaceutical products in the United States, only one has been approved in the past decade.¹⁴⁶

To illustrate this point a bit further, Pfizer, for example, spent over \$1 billion a year on drug discovery research between 2001 and 2010, but only brought forward four internally discovered drugs. This demonstrates that drug discovery is neither easy nor predictable, and it is no big surprise that the return on assets for the pharmaceutical industry is only around 5 percent—a figure much closer to industrial companies than to innovative and high-tech firms that prioritize R&D.

Offshoring of healthcare and biotech research jobs to China and India will probably continue for some time, although it will likely slow as the labor cost differential converges.

The success of the CRO/CMO industry shows that the model has clearly helped pharmaceuticals and biotech firms with their productivity problems. But whether this outsourcing model is a cure or just a panacea is still an open question.

Meanwhile, policymakers and consumers could increasingly adopt a “what we have now is good enough” attitude, accepting that existing and developing lines of generic drug

products cover a large enough therapeutic range that high levels of R&D are no longer necessary. This could leave government entities like the NIH to pick up slack for investment in R&D, which would likely focus on just a limited number of breakthrough drugs and treatments.

Epilogue¹⁴⁷

WX again attracted the attention of global investors in April 2010, when Charles River Laboratories announced that it had reached a deal to acquire WX for \$1.6 billion. The acquisition would have combined WX's experience in discovery and preclinical stages of drug development with Charles River's expertise in pre-clinical and clinical trials.¹⁴⁸

But the deal fell apart as analysts highlighted integration risks, given the disparate geographies and cultures and

questioned whether Charles River was overpaying. Investor pressure eventually killed the deal.

Meanwhile, WX's US testing business stabilized and actually returned to profitability in 2009. This segment earned \$64.1 million, which represented 2 percent annual growth on a pro-forma basis.¹⁴⁹ And it performed strongly in 2010, growing 18 percent to \$75.5 million. That same year, WX announced that it would reestablish biologics manufacturing services, only this time in China, using expertise gained from the defunct Philadelphia facility.¹⁵⁰

WX's China-based and US-based businesses have both continued to grow. By 2014, WX's total annual revenue had grown to \$674.3 million, with its US-based testing services accounting for \$99.6 million. By this time, WX had amplified AppTec's biologics and testing capabilities in China, and those segments generated \$42.6 million and \$124.3 million, respectively.¹⁵¹

Nor has WX's difficulty with the AppTec acquisition deterred it from pursuing additional M&As in China and the United States, as noted earlier. In 2011, WX acquired Abgent, a provider of biological research reagent products and services with a 34,000 square-foot facility in Suzhou and a 10,000 square-foot lab in San Diego, California.¹⁵²

In 2014, WX expanded its US testing business by acquiring XenoBiotic

Laboratories. This acquisition added 150 US employees and a 45,000 square-foot research center in New Jersey, strengthening its presence in bioanalytical and DMPK/ADME services, particularly in studies of radio-labeled compounds, and gaining the company access to new agricultural and animal health customers.¹⁵³ Finally, in 2015, WX acquired NextCODE, a genome sequencing company based in Cambridge, Massachusetts for \$65 million.¹⁵⁴

WX has also continued to expand its facilities in the United States. In April 2014, WX broke ground on an entirely new facility in Philadelphia to manufacture cell therapies, adding to its existing 16,000 square-foot facility. The expansion supported growing customer demand for allogeneic and autologous cell-based therapeutics.¹⁵⁵

The next month, in May 2014, WX completed another 20,000 square-foot materials characterization facility in St. Paul, Minnesota to expand its biologics testing services.¹⁵⁶ And in 2015, WX began the first phase of constructing yet another 145,000 square-foot facility in Philadelphia for manufacturing gene-mediated cell therapies, expected to be completed by mid-2016.¹⁵⁷

For all its challenges with the AppTec acquisition, WX seems to have regained its footing and is forging ahead after the financial crisis storm.

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The Paulson Institute's Program on Cross-Border Investment

There are compelling incentives for the United States and China to increase direct investment in both directions. US FDI stock in China was roughly \$60 billion in 2010, yet a variety of obstacles and barriers to further American investment remain. Meanwhile, Chinese FDI stock in the United States has hovered at around just \$5 billion. For China, investing in the United States offers the opportunity to diversify risk from domestic markets while moving up the value-chain into higher-margin industries. And for the United States, leveraging Chinese capital could, in some sectors, help to create and sustain American jobs.

As a nonprofit institution, The Paulson Institute does not participate in any investments. But by taking a sector-by-sector look at opportunities and constraints, the Institute has begun to highlight commercially promising opportunities—and to convene relevant players from industry, the capital markets, government, and academia around economically rational and politically realistic investment ideas.

The Institute's goal is to focus on specific and promising sectors rather than treating the question of investment abstractly. We currently have two such sectoral efforts—on agribusiness and manufacturing.

The Institute's aim is to help develop sensible investment models that reflect economic and political realities in both countries.

The Paulson Institute currently has four investment-related programs:

US-China Agribusiness Program

The Institute's agribusiness programs aim to support America's dynamic agriculture sector, which needs new sources of investment to spur innovation and create jobs. These programs include:

- A US-China Agricultural Investment Experts Group comprised of some of the leading names in American agribusiness. The group brainstorms ideas and helps in the Institute's effort to develop innovative investment models that reflect economic and technological changes in global agriculture.
- Periodic agribusiness-related investment workshops, bringing key players and companies together. The Institute held the first workshop in Beijing in December 2012. Attendees included CEOs and experts. It has since held smaller, sessions in the United States focused on specific technologies or aspects of agribusiness.

- Commissioned studies that propose specific investment models, including for commodities, such as pork, or value chain opportunities, such as collaborative research and development (R&D).

US-China Manufacturing Program

In June 2013, the Institute launched a program on trends that will determine the future of global manufacturing and manufacturing-related capital flows. We aim to identify mutually beneficial manufacturing partnerships that would help support job growth in the United States. The Institute's principal manufacturing programs include:

- Investment papers that the Institute is co-developing with private sector and academic partners.
- Periodic workshops in Beijing and Chicago with Chinese, American and global CEOs and executives, focused on technological change, sectoral trends, and investment opportunities.

Case Study Program

The Institute publishes in-depth historical case studies of past Chinese direct investments in the United States, examining investment structures and economic, political, and business rationales. These detailed studies are based on public sources but also first-hand interviews with deal participants on all sides. They aim to reconstruct motivations and actions, and then to draw lessons learned.

State-Level Competitiveness Program

The Institute works closely with several US governors to help them hone their teams' approach to attracting job-creating foreign direct investment. Our core competitiveness program is a partnership with states in the Great Lakes region, but we work with other governors as around the United States as well.

- Paulson Institute-Great Lakes Governors Partnership: Working closely with the Council of Great Lakes Governors, the Institute is honing pilot strategies to help match the "right" investors and recipients to the "right" sectoral opportunities. Work is also focusing on how to connect Great Lakes/St. Lawrence-based R&D and innovation to foreign deployment opportunities while opening markets in China. The Council includes the governors of Illinois, Indiana, Michigan, Minnesota, New York, Ohio, Pennsylvania, and Wisconsin, as well as the Canadian premiers of Ontario and Quebec.

- American Competitiveness Dialogues: The Institute convenes an ongoing series of competitiveness forums around the United States. These aim to address the implications of the changing global economy for US competitiveness, opportunities and challenges associated with foreign direct investment.
- R&D+Deployment (“R&D+D”): Working with partners, including McKinsey & Company and a small number of universities, the Institute is exploring new models that would link Chinese investors to the US innovation engine, especially in areas linked to demand-side needs in the China market. The aim is to design fresh models that capture value in both countries but do not sacrifice America’s innovation edge or intellectual property protection. Our dialogue in this area aims, ultimately, to lead to a pilot initiative.

About The Paulson Institute

The Paulson Institute, an independent center located at the University of Chicago, is a non-partisan institution that promotes sustainable economic growth and a cleaner environment around the world. Established in 2011 by Henry M. Paulson, Jr., former US Secretary of the Treasury and chairman and chief executive of Goldman Sachs, the Institute is committed to the principle that today's most pressing economic and environmental challenges can be solved only if leading countries work in complementary ways.

For this reason, the Institute's initial focus is the United States and China—the world's largest economies, energy consumers, and carbon emitters. Major economic and environmental challenges can be dealt with more efficiently and effectively if the United States and China work in tandem.

Our Objectives

Specifically, The Paulson Institute fosters international engagement to achieve three objectives:

- To increase economic activity—including Chinese investment in the United States—that leads to the creation of jobs.
- To support urban growth, including the promotion of better environmental policies.
- To encourage responsible executive leadership and best business practices on issues of international concern.

Our Programs

The Institute's programs foster engagement among government policymakers, corporate executives, and leading international experts on economics, business, energy, and the environment. We are both a think and "do" tank that facilitates the sharing of real-world experiences and the implementation of practical solutions.

Institute programs and initiatives are focused in five areas: sustainable urbanization, cross-border investment, climate change and air quality, conservation, and economic policy research and outreach. The Institute also provides fellowships for students at the University of Chicago and works with the university to provide a platform for distinguished thinkers from around the world to convey their ideas.

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5711 South Woodlawn Avenue
Chicago, IL 60637
paulsoninstitute.org