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The Medicines Company

"When people first hear our business concept, they think we're crazy," stated Clive Meanwell, the founder, president, and CEO of the Medicines Company. Formed in 1996, the Medicines Company "acquired, developed, and commercialized pharmaceutical products in late stages of development," meaning that it purchased the rights to drugs that other companies had abandoned. As Meanwell explained it:

> We founded our company on the premise that sometimes there is still value in drugs that fail to meet a developer's initial expectations. Companies develop drugs with particular applications, users, price points, and market sizes in mind. When clinical testing calls these expectations into question, companies often halt development. But drugs that seem unprofitable for one application or user group might prove quite profitable for others. Our job is to find such drugs, acquire them at reasonable prices, complete their development, and bring them to market.

By early 2001, this strategy seemed to be working. Four years earlier, the company had acquired the rights to Angiomax, a blood-thinning drug, or "anticoagulant," that Biogen had abandoned after $150 million and seven years of development. On December 17, 2000, after completing the required clinical trials, the Medicines Company received U.S. Food and Drug Administration (FDA) approval to sell the drug for use in conjunction with an artery-clearing procedure known as an angioplasty. (**Exhibit 1** provides a newspaper account of this drug approval.)

In spite of this good news, several issues remained for Meanwell and his management team. The first issue involved pricing. Angiomax was positioned as an alternative to "heparin," the most widely used anticoagulant in emergency coronary heart care. The problem was that heparin cost about $2 per dose. While it was clear that the Medicines Company would price Angiomax above heparin, the question was "how much above?"

The second issue involved the need to develop a product portfolio. Meanwell had long argued that the company's success depended on the development of a drug pipeline. However, the company had run into problems with its second acquisition—a migraine headache drug—and had halted its development. This setback and Angiomax's recent FDA approval had Meanwell wondering whether there truly was the need for a drug pipeline.

Finally, as a public company, the Medicines Company faced the realities of the stock market. In fact, many investors had expected a sharp stock price increase with the approval of Angiomax. Instead, the company's stock (Nasdaq: MDCO) fell over 25% in the month following FDA approval (see **Exhibit 2**). This caused some people to question the company's core business strategy.

Professor John T. Gourville prepared this case. HBS cases are developed solely as the basis for class discussion. Cases are not intended to serve as endorsements, sources of primary data, or illustrations of effective or ineffective management. Some nonpublic company data have been disguised and some business details have been simplified to aid in classroom discussion.

The Drug Development Industry [1]

By any measure, prescription drugs were big business. At the manufacturer level, prescription sales in 2000 approached $220 billion worldwide, with growth projected at 10% per year through 2010. The largest market for these drugs was the United States, accounting for 50% of all sales.

The United States was also home to most of the world's major drug companies (see **Exhibit 3**). The largest of them was Pfizer/Warner-Lambert, with annual drug revenues in excess of $25 billion worldwide and $14 billion domestically. As for profitability, the U.S. drug industry ranked first among all major industries, with net incomes at almost 20% of revenues in 1999.[2]

In 2000, several trends were impacting the U.S. drug market. They included:

- An aging population. In 1999, people aged 65 or over accounted for 15% of the population but 33% of prescription drug sales in the United States. Between 2000 and 2020, this population was expected to grow from 35 million to 55 million.
- Increased price pressure. Prescription drugs accounted for 9% of medical expenses in 2000 and were growing at a 20% annual rate. As a result, managed care organizations (which paid for 70% of all prescription drugs) and the government (which paid for 10%) were pressuring drug companies to contain or lower drug prices.
- The growth in generics. As a rule, a generic drug came to market soon after the patent on a branded drug expired, typically at a price 25% to 75% below the price of the branded drug. Between 2000 and 2010, generic sales were expected to grow from $10 billion to $60 billion as several blockbuster drugs came off patent.

Drug Development

Historically, new drugs were the lifeblood of the pharmaceutical industry, drugs under development at any point in time representing the potential blockbuster drugs that would drive the industry 5 to 10 years later. The successful development of a new drug was far from easy, however. Beginning in 1938, the FDA required drug developers to follow a complex process designed to prove the safety and effectiveness of any proposed new drug. Accordingly, pharmaceutical firms followed a sequential drug development process:

- In *preclinical/animal trials*, a candidate drug was identified, studied for its chemical properties, and tested on animals to assess safety and effectiveness. Most drugs were eliminated at this stage due to unacceptable side effects or failure to work as expected.
- In *Phase I clinical trials*, the drug was given to a small number of healthy people in order to test safety. Initially, small doses were administered, with dosage increased over time to assess safety at higher levels.
- In *Phase II clinical trials*, the drug was given to people suffering from the condition that the drug was intended to treat. This stage usually included a larger number of people and a longer period of time than in Phase I.

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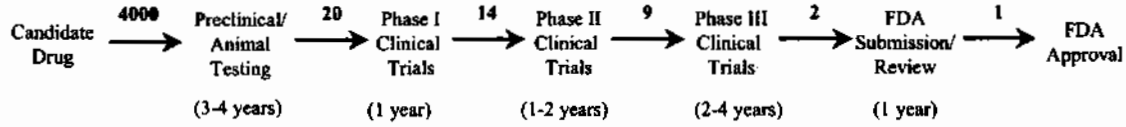
1 Much of these data were drawn from S&P's industry survey, "Healthcare: Pharmaceuticals," December 21, 2000.

2 "Health's Price Tag," *The Boston Globe*, March 28, 2001, p. D4.

- *Phase III clinical trials* were the most critical of the four stages.[3] They were the largest, most complex, and most rigorous of the human trials, designed to test fully the safety, effectiveness, and dosing levels of the drug on actual patients.
- An *FDA submission* typically followed a successful Phase III trial. It came in the form of a new drug application (NDA) seeking FDA approval for the commercial release of the drug. Each year, the FDA approved about half of all the NDAs it received.

This drug development process was remarkable in several respects. First, as outlined in **Figure A**, for every drug that received FDA approval, approximately 4,000 candidate drugs began the process. Second, the process took an average of 10 years to complete successfully. Third, the process was capital intensive, with U.S. drug companies spending $26 billion on drug development in 2000 (**Exhibit 4** provides a breakdown of how this money was spent). Finally, a company generally applied for (and received) a 20-year patent for a drug it had under development. After completing development, however, only about 10 to 15 years of patent protection remained (for instance, in the United States, the Angiomax patent was due to expire in 2010).

Figure A Stages of Drug Development (average years in each stage in parentheses)



These factors combined to create an industry that relied heavily on "blockbuster drugs"—premium-priced breakthrough drugs that generated in excess of $1 billion in sales per year. In 1999, 19 drugs met this threshold in the United States (see **Exhibit 5** for the 10 top-selling domestic prescription drugs). Meanwell described this focus on blockbuster drugs in the following fashion:

> In any given year, only about 90 drugs receive FDA approval. Across 40 drug companies, this means that the average drug firm is turning out only one or two new drugs a year—maybe three in a good year. If you are Merck, with over $10 billion in sales and your investors expect 10% growth per year, these one or two drugs have to generate a lot of revenue. A drug that brings in $200 million just won't do it for you.

The Medicines Company History

The Medicines Company was founded in July 1996 by Meanwell and a small group of investors on the premise that there was opportunity where other companies saw failure. Their corporate strategy was to acquire drugs that were in the late stages of product development but were undervalued by their developing companies. Once such drugs were acquired, the Medicines Company planned to complete product development, navigate the regulatory process, and commercialize the drugs in the United States and abroad.

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[3] Typically, Phase II and Phase III clinical trials were done across several hospitals, with doctors administering the candidate drug to a random sample of patients seeking treatment for the target disease. Quite often, the process was "double-blind," with neither the doctor nor the patient knowing what drug was administered.

While some questioned the logic of this business model, 15 years of experience in international drug development had convinced Meanwell that such a strategy made sense. As director of product development for Hoffman-LaRoche, one of Europe's largest drug developers, Meanwell had come to believe that drug firms often overreacted to clinical results, sometimes abandoning drugs that still had value. *The Boston Globe* described Meanwell and his company's business strategy as follows:

> You might say Dr. Clive Meanwell is a bit of a scavenger. ... After all, he founded a company four years ago based on the idea that there was money to be made off drugs other companies cast aside. His Cambridge start-up ... picks through and rescues products languishing because of lackluster results, shifting corporate priorities, or development problems.[4]

Of course, the first task for Meanwell and his colleagues was deciding what drugs to "rescue." To guide them in their acquisitions, Meanwell and his colleagues looked for drugs that met the following criteria:

- Required less than four years to get to market
- Required less than $60 million to get to market
- Had at least a 65% chance of getting to market
- Had the potential to generate at least $100 million per year in sales

Beginning in late 1996, the team spent six months reviewing potential acquisitions—starting with 3,000 candidates, quickly weeding those down to 20, and then seriously considering 3 or 4. By early 1997, they had settled on Angiomax, an anti-blood-clotting drug that Biogen had been developing as a more effective alternative to heparin, the anti-clotting drug most widely used in the acute treatment of coronary heart disease. In 1994, Biogen had halted development of Angiomax after clinical tests suggested that it was no more effective than heparin. Upon reviewing Biogen's clinical test results, however, Meanwell became convinced that a market still existed for the drug. Thus, in March 1997, the Medicines Company acquired all rights to Angiomax and set out to complete the clinical trials that Biogen had started. Finally, in December 2000, the Medicines Company received FDA approval for the use of Angiomax in the prevention of blood clots during a coronary procedure known as an angioplasty.

Following a similar screening process, in 1998 the Medicines Company acquired the rights to IS-159, a drug designed to treat acute migraine headaches. And in 1999 it acquired the rights to CTV-05, a drug designed to treat gynecological infections in women of childbearing age.

During its four-year effort, the Medicines Company relied upon two sources of funds. From its inception through mid-2000, the company received approximately $100 million in several rounds of funding from several private equity firms. Then, in August 2000, the company raised $101.4 million (after fees) from an initial public offering of 6,900,000 shares at $16 per share.

Through early 2001, these funds were used almost exclusively to acquire and develop the company's three drugs. In fact, through December 2000, the company had yet to report revenues of any kind (see **Exhibit 6**). At the same time, the company had close to $100 million in cash and short-term assets to finance the commercial launch of Angiomax and the continued development of its other products (see **Exhibit 7**).

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[4] "The Rescuers," *The Boston Globe*, September 13, 2000.

Angiomax

Without question, Angiomax was The Medicines Company's lead product, representing the company's first attempt at rescuing a seemingly failed drug. The specific application for which Angiomax received FDA approval was for the treatment of "high-risk" patients undergoing a balloon angioplasty. A balloon angioplasty was a procedure developed in the 1970s to restore normal blood flow to arteries in the heart clogged by a fatty buildup called plaque. In an angioplasty, a small incision was made in a blood vessel in the groin and a long flexible tube with a deflated balloon was threaded through an artery until it reached the clogged artery in the heart. The balloon was then inflated, compacting the plaque against the artery wall and opening the artery to increased blood flow.[5]

Sometimes, this procedure would lead to the formation of an unwanted blood clot in the area of the angioplasty. This blood clot had the potential to reclog the artery, leading to chest pains and a possible heart attack. Angiomax was designed to reduce the likelihood that such a clot would form.

Coronary Heart Disease

Through the late 20th century, coronary heart disease was the leading cause of death in the United States, accounting for 1 in every 5 deaths. It involved the narrowing of the arteries of the heart due to the gradual buildup of plaque on the inside of the artery walls. Over time, this buildup would narrow the artery and reduce the flow of blood and oxygen to the heart muscle, often resulting in chest pains following physical exertion. This type of pain was called stable angina.

Sometimes, a portion of the built-up plaque would tear or break off, triggering the rapid formation of a blood clot at the site of the tear. This blood clot would further reduce the flow of blood to the heart, causing steadier and more intense chest pains called unstable angina. In extreme cases, the blood clot would completely cut off the blood supply to the heart and cause a heart attack. If the blood supply were cut off for a long enough period, the cells of the heart would die, leading to permanent disability or death.

By the late 1990s, an estimated 14 million Americans had some form of coronary heart disease, 7 million of whom suffered from stable angina. Of these, about 1.5 million experienced unstable angina each year, another 1.1 million suffered a full-blown heart attack, and close to 500,000 died.

While patients suffering from stable angina were treated with a regimen of diet, exercise, and a variety of slow-acting drugs, patients with unstable angina or full-blown heart attacks required emergency care. Typically, such patients immediately received a combination of several fast-acting drugs, including TPA, which was meant to break apart the clot that had formed, and an anticoagulant, which was meant to prevent a new clot from forming.

Shortly after this initial treatment, most emergency care patients underwent either a balloon angioplasty or coronary artery bypass surgery (CABG), which involved surgically replacing the clogged coronary arteries with healthy blood vessels taken from the patient's leg. In 1999, roughly 700,000 angioplasties and 400,000 CABGs were performed in the United States. Both types of operations had the potential to further disrupt arterial plaque, leading to the formation of a new

[5] In about 65% of cases, in addition to the angioplasty, a small metal mesh tube called a stent was threaded through the artery and placed at the site of the blockage. This tube was meant to permanently prop open the artery to restore blood flow.

blood clot. Therefore, anticoagulants also were widely administered to prevent blood clots from forming before, during, and after these procedures.

Heparin

By far, the most widely prescribed anticoagulant in acute coronary heart treatment was heparin. Discovered in 1916, heparin was initially used to prevent the coagulation of blood samples drawn from patients. By the 1990s, however, it was the primary drug used to prevent unwanted blood clots from forming as the result of unstable angina, heart attacks, and coronary surgery. Having never been subject to patent protection, heparin was viewed as a commodity drug and sold by many different manufacturers at about $2 per vial. As reflected in **Table A**, Meanwell estimated that about 3.5 million coronary care patients received heparin each year to prevent unwanted blood clots.

Table A Heparin Use Across Treatments

Treatment	# of Patients Per Year Receiving Drug
Unstable Angina (i.e., elevated chest pains)	1,300,000
Heart Attack	1,000,000
Balloon Angioplasty	700,000
Coronary Artery Bypass Surgery	400,000
Other	100,000

Source: Medicines Company estimates.

Despite its almost universal use, heparin was not without it shortcomings, however, as Meanwell was quick to point out. These included:

- Unpredictability. Both within and across patients, the anticlotting effect of heparin was unpredictable. Its use required very close monitoring.
- High risk of bleeding. Some patients who received heparin had a high incidence of uncontrolled bleeding.
- Adverse reaction. In 2% to 3% of patients, heparin caused a sometimes fatal immune reaction called heparin-induced thrombocytopenia or HIT.

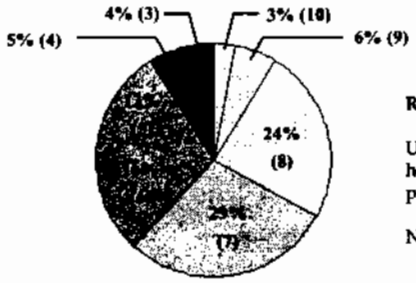
These shortcomings led some medical experts to question the ongoing use of heparin. As one cardiologist pointed out:

> Heparin is easy to use, but difficult to use properly. Its effectiveness depends on achieving a certain degree of anticoagulation in the blood. Too much anticoagulation and the patient can suffer from uncontrolled bleeding. Too little anticoagulation and you might not prevent a blood clot. But that window of proper dosing differs across patients and across time. As a result, you need to monitor the patient very closely. Making the problem more complex, it takes several hours for the effects of heparin to kick in and wear off. This means that you might have to wait three or four hours to see if a given dose of heparin has the desired effect.[6]

[6] Reflects comments obtained from a cardiologist in interviews conducted by the Medicines Company.

To assess the prevalence of this viewpoint, the Medicines Company conducted a random survey of 90 leading interventional cardiologists (the doctors who perform angioplasties) that asked them to rate their satisfaction with heparin. (Results of this survey are shown in **Figure B**.)

Figure B Overall Satisfaction with Heparin among Interventional Cardiologists



Responses to the Question:

Using a 10-point satisfaction rating scale, please rate your overall satisfaction with heparin as an anticoagulant when administered during a balloon angioplasty procedure. (1 = Not at all satisfied; 10 = Extremely satisfied)

Numbers indicate the percentage of doctors reporting the rating shown in parentheses.

Source: Company Records

Biogen's Angiomax: A Replacement for Heparin

Angiomax began its life in the mid-1980s in the laboratories of Biogen. Biogen's insight into Angiomax began with the observation that certain animals, such as leeches, drew blood from their victims without triggering the victim's blood-clotting process. Armed with this insight, Biogen isolated the chemicals in leech saliva that caused this anticlotting response. Once isolated, Biogen was able to reproduce it using recombinant technologies.

As initially conceived, Angiomax was to replace heparin for use during angioplasties. According to Meanwell, Biogen expected the typical angioplasty patient to require about four doses of the drug. Longer term, Biogen hoped Angiomax would replace heparin in almost all applications.

Over the next 7 years, Biogen spent $150 million bringing Angiomax through to Phase III trials. In 1994, however, Biogen came to two unsettling conclusions. First, its Phase III clinical trial involving "high-risk" angioplasty patients suggested that Angiomax was only slightly better than heparin at preventing blood clots. Second, given the complexity of the drug, Biogen expected that it would cost $100 per dose to produce Angiomax. In an industry where the typical "price" to "cost of goods sold" ratio was 10 to 1, this implied a selling price of $1,000 per dose. Reluctantly, Biogen halted development of Angiomax, concluding that its benefits did not justify such a price. Meanwell described Biogen's decision as follows:

> In 1994, Biogen was at a bit of a crossroads. To that point, they had licensed products to other drug companies. But, in the summer of '94, they had two drugs in Phase III trials—their first attempts to bring a product to market. One was Angiomax. The other was Avonex, a drug to treat multiple sclerosis. In July, the Phase III Avonex study showed very promising results. Then, in September, the Phase III Angiomax study showed mixed results. As a result, Biogen decided to pour its resources into Avonex and to shelve Angiomax. In the end, this may have been the right decision. Biogen received FDA approval for Avonex in 1996 and quickly turned it into the world's best-selling multiple sclerosis drug. In 2000, they sold over $750 million worth of Avonex.

The Decision to Acquire Angiomax

Following its decision to shelve Angiomax, Biogen actively shopped the drug to other biotech and pharmaceutical firms in the hopes that one would acquire or license the drug. One such firm was Hoffman-LaRoche, where Meanwell was head of drug development. While he decided not to pursue Angiomax, two things struck Meanwell about the drug. First, although the drug was not as effective as Biogen would have liked, it still was more effective than heparin. Second, if the cost to produce the drug could be reduced by half, the economics became attractive.

Several years later, Angiomax once again came across Meanwell's radar screen as the Medicines Company searched for its first acquisition. Remembering his initial impressions of the drug, the team reanalyzed Biogen's Phase III results. (These results are shown in **Table B.**) Biogen's study had involved 4,312 "high-risk" angioplasty patients, with half receiving Angiomax and half receiving heparin. For this study, patients were defined as "high-risk" if they had previously had a heart attack or if they were admitted to the hospital because of unstable angina. On average, such "high-risk" patients accounted for about 50% of all angioplasty patients.[7]

Table B Phase III Results for "High-Risk" Patients Undergoing an Angioplasty

Outcome within 7 days of treatment (number of patients in condition)	Heparin (2,151)	Angiomax (2,161)
Death	0.2%	0.2%
Heart Attack	4.2%	3.3%
Need for a Repeat Angioplasty	2.8%	2.5%
Experienced Major Bleeding	9.3%	3.5%

Source: The Medicines Company.

In addition, the Medicines Company found that for a particular subgroup of "high-risk" patients—those who had experienced a heart attack in the two weeks immediately preceding the angioplasty—the benefits of Angiomax were more pronounced. (**Table C** provides a comparison of heparin and Angiomax for these "very high-risk" patients.) On average, these patients represented 20% of the "high-risk" patients (or 10% of all angioplasty patients).

Table C Phase III Results for "Very High-Risk" Patients

Outcome within 7 days of treatment (number of patients in condition)	Heparin (372)	Angiomax (369)
Death	0.5%	0.0%
Heart Attack	5.6%	3.0%
Need for a Repeat Angioplasty	3.5%	2.4%
Experienced Major Bleeding	11.8%	2.4%

Source: The Medicines Company.

[7] For the remaining 50% of angioplasty patients—that is, "low-risk" patients—Meanwell estimated that the relative benefits of Angiomax over Heparin were about half as great as those shown in **Table B.**

When asked to account for these results, Meanwell noted that Angiomax did not have many of the drawbacks that heparin had. Specifically, he noted:

> Unlike those of heparin, the effects of a dose of Angiomax are very exacting and very crisp. Physicians who use Angiomax have been pleasantly surprised by how predictable their results are, which is important in an acute-care setting where you are trying to minimize uncertainty. Second, the product works better among patients at risk for bleeding, where heparin often proves problematic. Third, the product works faster than heparin. Instead of taking 2 to 3 hours to take full effect, Angiomax only takes 30 minutes. Finally, there is no immune reaction to Angiomax, so you don't have to worry about unexpected reactions to the drug. These benefits seem to have the greatest impact for the "very high-risk" patients.

Based on their reanalyses, Meanwell and his colleagues agreed to acquire all rights to the drug's formulation, its manufacturing specifications, and its clinical trial results. These clinical trial results included the Phase III results for angioplasty but also included Phase II results for studies looking at the impact of Angiomax in the treatment of heart attack, unstable angina, and heparin-induced thrombocytopenia (HIT).

The cost of this acquisition was an up-front fee of $2 million, a commitment to invest another $28 million in the continued development of the product, and a future royalty that started at 6% of sales and rose to 20% of sales as sales volumes increased.

Bringing Angiomax to Market

Upon acquiring Angiomax in 1997, the Medicines Company set out to address several issues. First, the company conducted a confirmatory clinical study using "high-risk" angioplasty patients, obtaining results similar to those shown in **Table B**. On the combined strength of Biogen's initial studies and this confirmatory study, the Medicines Company submitted a new drug application (NDA) in early 2000 and on December 17, 2000, obtained FDA approval to market Angiomax for use in "high-risk patients undergoing a balloon angioplasty." Meanwell estimated that the Medicines Company spent a total of $12 million in finishing these clinical trials and gaining FDA approval.

The second thing that the company did was to focus on bringing down the cost of using Angiomax. This was accomplished in two ways. First, rather than four doses of Angiomax, further clinical testing revealed that about 70% of angioplasty patients would require a single dose, with the other 30% requiring two or three doses. Second, in 1999 the Medicines Company contracted out production of Angiomax to UCB Bioproducts, with the understanding that UCB would attempt to develop a second-generation manufacturing process to bring down the cost of production. The Medicines Company contributed almost $10 million to this development effort. The result was a new production process that reduced the cost of goods sold from $100 per dose to about $40 per dose.

The third thing the company did was to push forward on the other Angiomax clinical trials. In particular, it undertook additional studies to confirm the benefits of Angiomax (1) for patients experiencing heart attacks and unstable angina, (2) for patients at risk for HIT, and (3) for patients undergoing coronary artery bypass surgery. By early 2001, the company had five sets of clinical trials either completed or under way, as reflected in **Exhibit 8**.

The Marketing of Angiomax

Making the case for Angiomax As it became apparent that Angiomax would gain FDA approval, the company's next big task was to establish a "going to market" strategy for the drug. As part of this strategy, the company hired Dr. Stephanie Plent as senior director of medical policy. Part of Plent's job was to communicate the benefits of Angiomax to cardiologists and hospital administrators. She explained these benefits in the following fashion:

> When a hospital performs an angioplasty on a patient covered by insurance, it is reimbursed at a predetermined rate. Currently, that rate is $11,500. In most cases, this more than covers the cost of the procedure—an angioplasty with no complications costs a hospital about $9,500 to perform.
>
> In a small percentage of cases, however, complications do arise. But insurance companies do not reimburse the cost of these complications. Instead, hospitals are forced to absorb these added expenses. On average, a hospital incurs an additional $8,000 to treat a person who has a heart attack, requires a repeat angioplasty, or experiences major bleeding. These added costs are largely due to the fact that the patient's hospital stay is extended by four or five days. Even a death costs the hospital an additional $8,000. Angiomax helps avoid some of these costs.

At the same time, Plent noted that this message had a different impact on the various members of the hospital staff. She pointed out that there were three major groups that influenced the purchase and use of any new drug: (1) the doctor who would use the drug, (2) the hospital pharmacist who would carry the drug, and (3) the hospital administrator who would approve the drug for ongoing use within the hospital. Each of these groups had a different set of incentives, as Plent pointed out:

> Selling a premium-priced new drug into a hospital is a tricky process. First, there are the doctors. You have to convince them that the drug works. They are not concerned with price so much as they are with results. Next, there are the hospital pharmacists. They have an annual budget for all the drugs they dispense and are rewarded for meeting or beating that budget. Replacing a widely used $10 drug with a $100 drug really kills that budget. Unless they can justify the cost of the new drug to the hospital administrators and get the added expense incorporated into their budgets, it is unlikely they will carry it. Finally, there are the hospital administrators. They take the big picture into account—does this drug make economic sense. Unfortunately, drug companies rarely have direct access to these administrators. Rather, we have to work through the doctors and the pharmacists and get them to push for the drug.

Assembling a sales force The task of selling Angiomax into this complex network of hospital personnel fell to Tom Quinn, vice president of sales and marketing. It was Quinn's job to assemble a sales force, promote the use of Angiomax, and ramp up sales over time.

According to Quinn's analysis, 1,300 medical centers around the country performed angioplasties, with the typical center staffed by 5 to 20 interventional cardiologists. Across these 1,300 centers, Quinn decided to focus on those 700 centers responsible for 92% of all angioplasty procedures. These 700 angioplasty centers were divided into five sales regions.

To service each of these five regions, Quinn hired a regional manager and outsourced to a marketing services firm for 10 to 15 account reps. Quinn explained his thinking behind this approach:

> When we looked at what we needed to do, we realized we needed people with existing relationships within the acute coronary care community. Also, we wanted to ramp up rapidly. The answer was Innovex, a marketing services firm. They provided us with fully dedicated salespeople with an average of 5 years of sales experience and with existing relationships with the doctors and pharmacists we wanted to reach. As for our regional managers, we hired them as Medicines Company employees to retain control and to create stability over time.

Quinn was also responsible for educating the marketplace. This included publication of academic journal articles, presentations at trade shows, and the advertising of Angiomax in medical journals. Beginning in the fall of 2000, for instance, Quinn's marketing department started drawing attention to the shortcomings of heparin. Such an approach was made necessary by FDA regulations that forbade the marketing of a drug not yet approved for use. Therefore, at medical trade shows and in medical journals in October, November, and December, the company presented material designed to get doctors to question the safety of heparin. One such bit of material was an academic article on the deficiencies of heparin that appeared in the *Journal of Invasive Cardiology*. Once Angiomax was approved, the company followed with trade show presentations, journal articles, and advertisements in medical journals identifying Angiomax as the preferred alternative to heparin. (**Exhibit 9** provides an example of one such ad.)

Finally, Quinn sought to create advocates within the medical community. Through early 2001, the company sponsored four weekend getaways for thought leaders (and their families) in the cardiology community. These invitees were handpicked by the sales force and included 400 cardiologists, 75 nurses, and 30 pharmacists. Over the course of two days, they would participate in about eight hours of presentations designed to educate them on the company and the product. Quinn estimated that the Medicines Company spent about $3 million on these efforts.

Other Drugs Under Development by the Medicines Company

In addition to Angiomax, the Medicines Company had acquired two other "abandoned" drugs. In July 1998, the company acquired the rights to IS-159, a nasal spray designed to treat acute migraine headaches. And in August 1999, it acquired the rights to CTV-05, a drug designed to treat gynecological infections in women of childbearing age.

IS-159

Acquired from Immunotech S.A. of France, IS-159 was an acute migraine drug in Phase II trials that promised rapid absorption into the bloodstream. Under the acquisition agreement, the company paid an up-front fee of $1 million, was obligated to pay an additional $4.5 million upon reaching certain development milestones, and would pay a 5% royalty on sales upon commercialization of the product. At the time of the acquisition, Meanwell noted that the drug had shown promise in its Phase II trials, offering "an impressively rapid onset of action and a convenient form of administration." At that time, Meanwell estimated the migraine drug market to be about $2 billion.

By mid-1999, however, development of IS-159 had been halted by the Medicines Company. After spending an additional $6 million in clinical trials, the company had run into problems with the drug's formulation. Specifically, for the nasal spray to be absorbed into the bloodstream, an additive was needed. The additive being used was modified coconut oil. However, while modified coconut oil had gained FDA approval as an additive in oral medications, it had not yet gained FDA approval as an additive in nasal medications. As a result, the company faced the daunting task of either finding a new additive or conducting clinical trials to show the safety and effectiveness of coconut oil as a nasal additive. Meanwell estimated that either course of action would cost as much as $30 million and take five years.

CTV-05

With Angiomax looking like it would gain FDA approval, the failure of IS-159 in mid-1999 presented a problem. With plans to go public in the near future, all parties felt that it was critical to have a second drug under development to avoid the appearance that the company was a one-drug enterprise. IS-159 was supposed to have been that other drug. With its failure, the company was forced to rescue some other drug that was underappreciated.

That drug turned out to be CTV-05, a drug designed to treat bacterial vaginosis (BV), an infection common in women of childbearing age. By one estimate, 10% to 15% of college-age women suffered from BV, which often resulted in premature termination of pregnancies and in low-birth-weight babies. Under the terms of the acquisition, the Medicines Company obtained worldwide rights to the drug for an up-front fee of $1 million and future royalties of about 5%.

Upon reflection, Meanwell noted that the company's acquisition of CTV-05 was quite different from the company's earlier acquisitions. As he pointed out:

> With Angiomax, we knew the drug worked. Even with IS-159, we knew the drug worked—we just hadn't anticipated problems with its formulation. With CTV-05, we were taking a bit of a flier. We needed another drug under development, but there were no obvious alternatives. We didn't know if CTV-05 worked—it was only in Phase I trials—but we knew we could get it at low cost. So far, we have been happy with the results. We have invested about $4 million and we are currently completing Phase II trials. What started out as a high-risk investment is showing a lot of promise.

Looking Ahead

Moving forward, Meanwell knew that he and his colleagues had several decisions to make. First, they had to decide on the pricing of Angiomax. On the one hand, he felt that the product warranted a vast premium over heparin. On the other hand, he knew that replacing a widely accepted $2 drug with *any* drug costing many times more would raise a few eyebrows. Second, he had to decide whether the business strategy that brought the company to this point still made sense moving into the future. In particular, while a productive drug pipeline would be a nice thing to have, was it essential? Finally, Meanwell wondered how success with Angiomax would change the company and its underlying business model.

For the moment, however, Meanwell and his colleagues enjoyed the feeling of having rescued a drug with the potential to make a difference in people's lives.

Exhibit 1 Excerpt from *The Boston Globe*, December 19, 2000

Medicines Co. Receives FDA Approval for Blood Thinner

Drug up against cheaper heparin

by Naomi Aoki
Globe Staff

Medicines Co. yesterday said it won regulatory approval to market its first product, a blood thinner designed as an alternative to the 85-year-old standard treatment, heparin.

The drug, called Angiomax, was approved by the US Food and Drug Administration for use in an artery-clearing procedure known as angioplasty. The drug was developed to prevent blood clots that can lead to heart attacks.

... Angiomax [is expected to be] significantly more expensive than heparin, which sells at about $10 a vial. But the Cambridge company said data from more than 4,300 patients [showed the drug to be a superior alternative to heparin].

"Obviously, this is a very major milestone for Medicines Co.," said Dr. Clive Meanwell, the company's president and chief executive. "We think it is also a major milestone for the field of interventional cardiology. But most of all, we think it should be a significant milestone for patients."

Meanwell also hailed the approval as a confirmation of the young company's business model, based on the idea that there is money to be made off drugs that other companies cast aside.

Since other companies bring the products through the early stages of development, Medicines Co. bears less risk. Still, there is no guarantee that the products—sometimes shelved because of lackluster test results or unresolved developmental problems—will get to market.

In fact, at one time, the deck seemed stacked against Angiomax. The drug was discovered by Biogen Inc., among the nation's oldest and biggest biotechnology companies, but was abandoned after disappointing results from broad-based clinical trials.

Biogen's disappointment became Medicines Co.'s first project. The company licensed the drug from Biogen in 1997. ...

Jay B. Silverman, a senior biotech analyst with Robertson Stephens Inc. in New York, said he expects Angiomax to perform well against heparin. ... The challenge will be to persuade doctors and hospitals to change from heparin to Angiomax, he said, efforts that are already underway.

"That is always the challenge with these hospital products," Meanwell said. "Doctors are appropriately demanding of the data. They want to know how this drug will impact practices and costs."

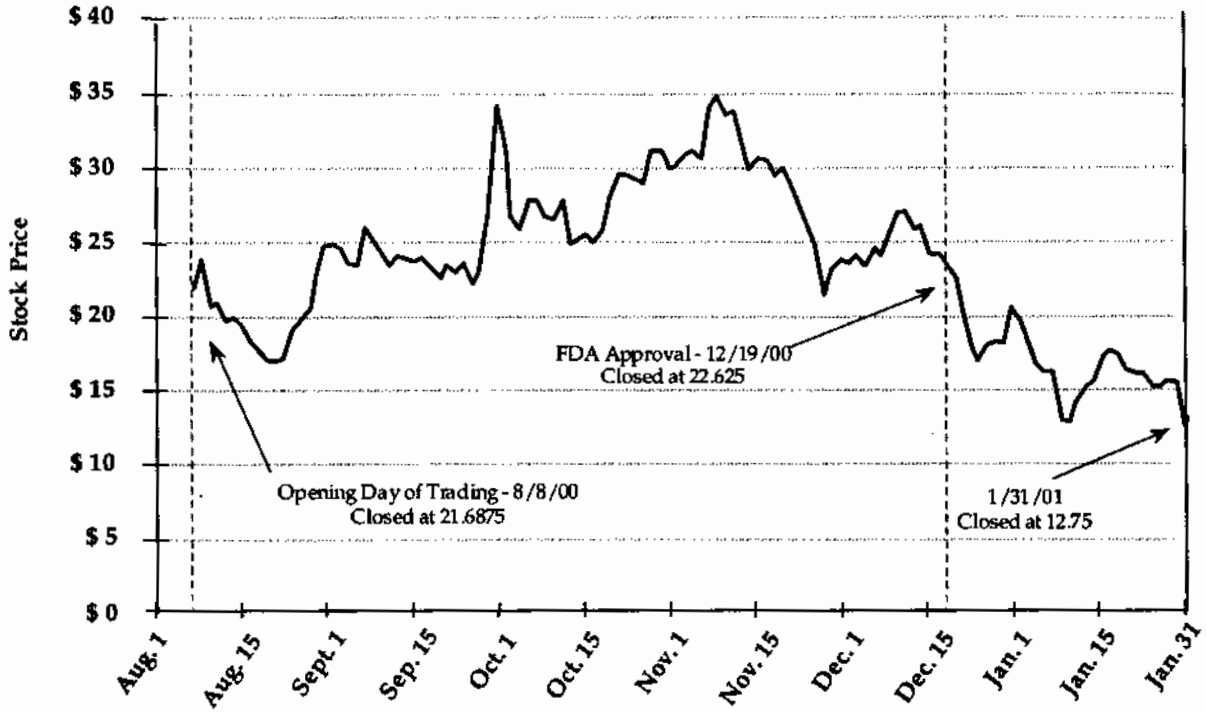
The company has plans to conduct clinical trials at hundreds of hospitals nationwide to allow doctors to gain hands-on experience with the drug, Meanwell said. It anticipates a series of articles to be published in upcoming issues of independent, peer-reviewed scientific journals.

Meanwell said the company has gathered a team of experienced sales and marketing executives to head the 52-person sales force. And the product will be launched officially next month, after a weeklong educational meeting for the sales staff. ...

"This approval is about the best Christmas present I could get," Meanwell said. "We're very excited, very relieved, and very grateful."

Source: *The Boston Globe*, December 19, 2000, p. C3.

Exhibit 2 The Medicines Company Stock Performance—August 8, 2000 to January 31, 2001



Source: Adapted from Web site, http://finance.yahoo.com.

Exhibit 3 Leading Pharmaceutical Companies, Ranked by U.S. Sales (in millions)[a]

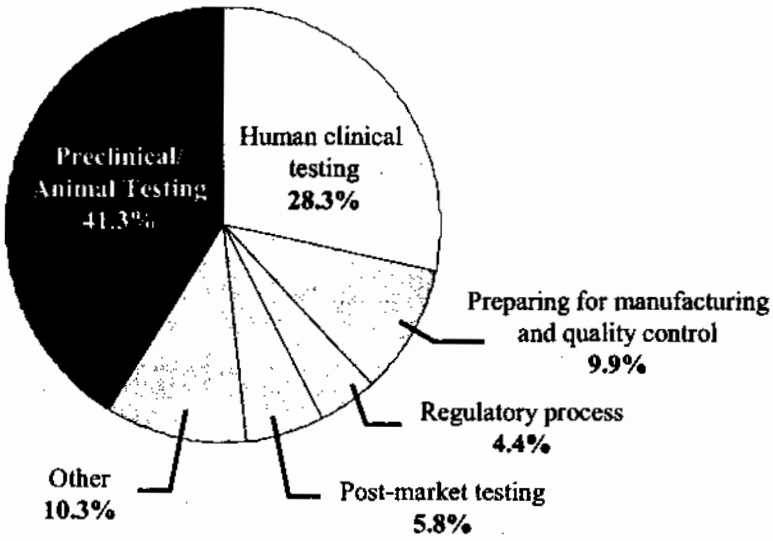
Company (Headquarters)	U.S. Sales
Pfizer/Warner-Lambert (U.S.)	$ 14,607
Glaxo Wellcome/SmithKline (U.K.)[b]	12,490
Merck (U.S.)	10,486
Bristol-Myers Squibb (U.S.)	8,778
Astra/Zeneca (U.K.)	8,304
Johnson & Johnson (U.S.)	7,636
Eli Lilly (U.S.)	6,173
Pharmacia (U.S.)	6,055
American Home Products (U.S.)	5,832
Schering Plough (U.S.)	5,716

Source: Standard & Poor's industry survey, "Healthcare: Pharmaceuticals," December 21, 2000.

[a] For 12 months ending September 30, 2000.

[b] Merger pending.

Exhibit 4 The Allocation of $26 Billion in Research and Development in 2000



Source: "Health's Price Tag," *The Boston Globe*, March 28, 2001, p. D4.

Exhibit 5 Best-Selling Prescription Drugs in the United States in 1999

Drug (Company)	Use	Retail Sales (in millions)
Prilosec (Astra/Zeneca)	Anti-Ulcer	$ 4,187
Lipitor (Warner Lambert)	Cholesterol Reducer	3,002
Prozac (Eli Lilly)	Antidepressant	2,571
Prevacid (TAP)	Anti-Ulcer	2,364
Zocor (Merck)	Cholesterol Reducer	2,301
Epogen (Amgen)	Red Blood Cell Stimulant	1,842
Zoloft (Pfizer)	Antidepressant	1,737
Claritin (Schering Plough)	Antihistamine	1,534
Paxil (SmithKline Beecham)	Antidepressant	1,516
Zyprexa (Eli Lilly)	Antipsychotic	1,495

Source: Standard & Poor's industry survey, "Healthcare: Pharmaceuticals," December 21, 2000.

Exhibit 6 The Medicines Company Operating Income: 1997 to 2000

	1997	1998	1999	2000
Revenue from Operations:	$0	$0	$0	$0
Operating Expenses:				
Research & Development	$ 16,044,367	$ 24,004,606	$ 30,344,892	$ 39,572,297
Sales, General & Administrative	2,420,373	6,248,265	5,008,387	15,033,585
Total Operating Expenses:	$ 18,464,740	$ 30,252,871	$ 35,353,279	$ 54,605,882
Loss From Operations:	($ 18,464,740)	($ 30,252,871)	($ 35,353,279)	($ 54,605,882)

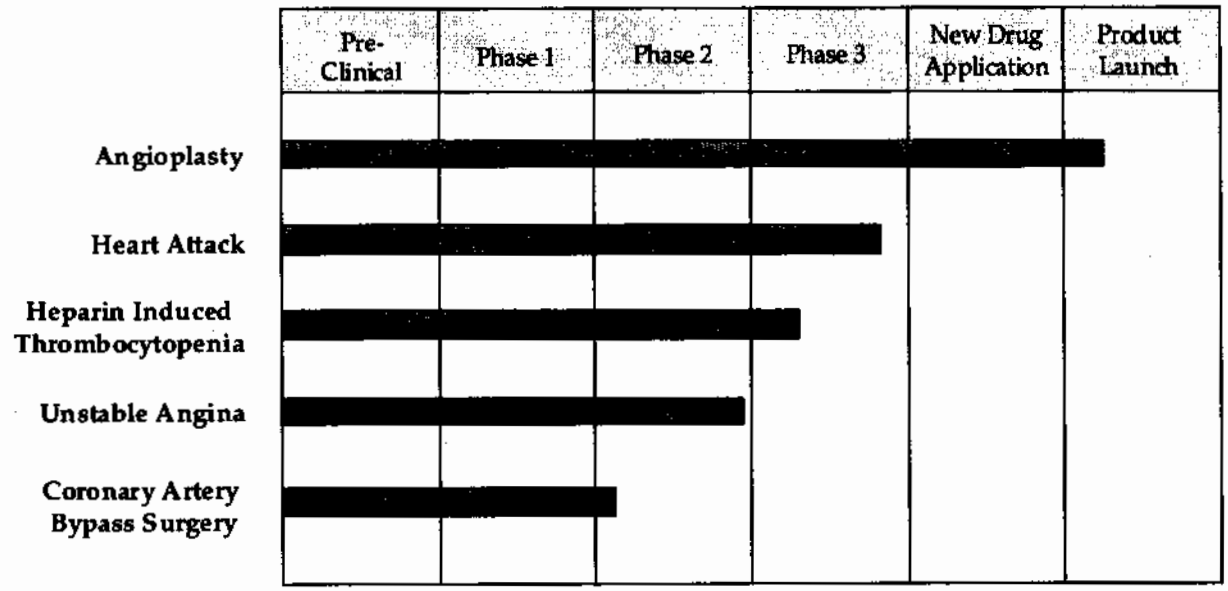
Source: Company records.

Exhibit 7 The Medicines Company Balance Sheet: 1999 and 2000 (FY ending December 31)

	1999	2000
Assets:		
Cash, Cash Equivalents, and		
Marketable Securities	$ 7,237,765	$ 80,718.013
Inventory	0	1,963,491
Fixed Assets (Net)	430,061	965,832
Other Assets	323,572	715,794
Total Assets:	$ 7,991,398	$ 84,363,130
Liabilities and Stockholders' Equity:		
Current Liabilities	$ 11,495,321	$ 15,124,147
Long-Term Liabilities	91,053,732	0
Stockholders' Equity (Deficit)	(94,557,655)	69,238,983
Total Liabilities and Stockholders' Equity:	$ 7,991,398	$ 84,363,130

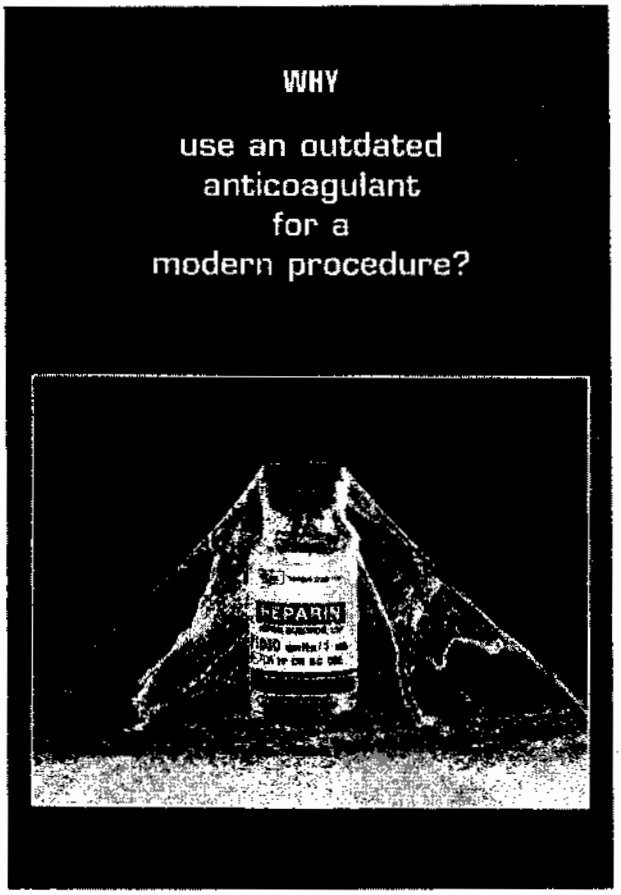
Source: Company records.

Exhibit 8 Status of Angiomax Clinical Trials



Source: The Medicines Company 2000 Annual Report.

Exhibit 9 An Example of a Two-Page Angiomax Ad—January 2001



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Source: Company documents.