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Biopure Corporation

It was February 5, 1998, as Carl Rausch, president and CEO of Biopure Corporation, opened his Boston Globe and read about the U.S. government's final approval of Oxyglobin (see **Exhibit 1**). Oxyglobin was the first of two new "blood substitutes" on which Biopure's future depended—Oxyglobin for the veterinary market and Hemopure for the human market. While Oxyglobin was ready for launch, Hemopure was still two years away from final government approval. This timing was the source of an ongoing debate within Biopure.

Ted Jacobs, vice president for Human Clinical Trials at Biopure, argued that the release of Oxyglobin should be delayed until *after* Hemopure was approved and had established itself in the marketplace (see **Exhibit 2** for an organizational chart of Biopure). Given that the two products were almost identical in physical properties and appearance, he felt that Oxyglobin would create an unrealistic price expectation for Hemopure if released first. As he made clear in a recent management meeting,

> ... [T]he veterinary market is small and price sensitive. We'll be lucky to get $150 per unit. The human market, on the other hand, is many times larger and we can realistically achieve price points of $600 to $800 per unit. But as soon as we come out with Oxyglobin at $150, we jeopardize our ability to price Hemopure at $800. Hospitals and insurance firms will be all over us to justify a 500% price difference for what they see as the same product. That's a headache we just don't need. We've spent $200 million developing Hemopure—to risk it at this point is crazy. We should just shelve Oxyglobin for now.

At the same time, Andy Wright, vice president for Veterinary Products, had his sales organization in place and was eager to begin selling Oxyglobin. He argued that the benefits of immediately releasing Oxyglobin outweighed the risks,

> Oxyglobin would generate our first revenues ever—revenues we could use to launch Hemopure. And while the animal market is smaller than the human market, it is still attractive. Finally, I can't stress enough the value of Oxyglobin in learning how to "go to market." Would you rather make the mistakes now, with Oxyglobin, or in two years, with Hemopure?

Professor John Gourville prepared this case as the basis for class discussion rather than to illustrate either effective or ineffective handling of an administrative situation. Some nonpublic data have been disguised and some business details have been simplified to aid in classroom discussion.

While Carl Rausch listened to this debate, he also considered his colleagues' growing desire to take Biopure public in the near future. He wondered whether a proven success with Oxyglobin might not have a greater impact on an IPO than the promise of success with Hemopure.

An Overview of Biopure

Biopure Corporation was founded in 1984 by entrepreneurs Carl Rausch and David Judelson as a privately owned biopharmaceutical firm specializing in the ultrapurification of proteins for human and veterinary use. By 1998, this mission had taken Biopure to the point where it was one of three legitimate contenders in the emerging field of "blood substitutes."[1] Blood substitutes were designed to replicate the oxygen-carrying function of actual blood, while eliminating the shortcomings associated with the transfusion of donated blood. Through the end of 1997, no blood substitute had received approval for use anywhere in the world.

Biopure's entries into this field were Hemopure, for the human market, and Oxyglobin, for the animal market. Both products consisted of the oxygen-carrying protein "hemoglobin" which had been removed from red blood cells, purified to eliminate infectious agents, and chemically modified to increase its safety and effectiveness. What distinguished Hemopure and Oxyglobin from other "hemoglobin-based" blood substitutes under development was the fact that they were "bovine-sourced" as opposed to "human-sourced"—they were derived from the blood of cattle. To date, Biopure had spent over $200 million in the development of Oxyglobin and Hemopure and in the construction of a state-of-the-art manufacturing facility.

Both of Biopure's products fell under the approval process of the United States government's Food and Drug Administration (FDA), which required that each product be proven safe and effective for medical use (see **Exhibit 3** for an overview of the FDA approval process). In this regard, Oxyglobin had just received final FDA approval for commercial release as a veterinary blood substitute, while Hemopure would soon enter Phase 3 clinical trials and was optimistically expected to see final FDA approval for release as a human blood substitute sometime in 1999.

This recent FDA approval of Oxyglobin brought to a peak a long-simmering debate within Biopure. With its primary goal being the development of a human blood substitute, Biopure's entry into the animal market had been somewhat opportunistic. During Pre-Clinical trials for Hemopure, the benefits of a blood substitute for small animals became apparent. In response, Biopure began a parallel product development process which resulted in Oxyglobin. However, there was little question within Biopure that Oxyglobin was an ancillary product to Hemopure.

As it became apparent that Oxyglobin would gain FDA approval prior to Hemopure, Carl Rausch and his management team discussed how best to manage Oxyglobin. As the first "blood substitute" of any type to receive full government approval, Rausch was eager to get the news out. With this in mind, Andy Wright and a small marketing team had been assembled to bring Oxyglobin to market. However, Ted Jacobs and others questioned whether the immediate release of Oxyglobin might not impinge on Biopure's ability to optimally price Hemopure. After months of debate, it was time to decide on the fate of Oxyglobin.

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[1] While the term *blood substitute* has historically been used to describe this class of product, Biopure and the medical community increasingly have used the term *oxygen therapeutic* to describe the latest generation of product. For simplicity, however, we will continue to use the term *blood substitute* in this case.

The Human Blood Market

Blood is essential for life. It performs many functions, the most acutely critical of which is the transportation of oxygen to the organs and tissues of the human body. Without oxygen, these organs and tissues will die within minutes.

That portion of blood responsible for oxygen transportation are the red blood cells (RBCs). RBCs capture inhaled oxygen from the lungs, carry that oxygen to the cells of the body, release it for use where needed, capture expended carbon dioxide from those cells, and carry that carbon dioxide back to the lungs, where it is released. The key to this process is "hemoglobin," the iron-containing protein found within each RBC to which oxygen and carbon dioxide molecules bind.

The adult human body contains 5,000 milliliters (ml) or about 10 pints of blood. An individual can naturally compensate for the loss of up to 30% of this volume through some combination of increased oxygen intake (i.e., faster breathing), increased flow of the remaining blood (i.e., faster heart rate) and the prioritization of blood delivery to vital organs. In cases of blood loss of greater than 30%, however, outside intervention is typically required—generally in the form of a "blood transfusion."

Human Blood Transfusions

A blood transfusion entails the direct injection of blood into a patient's bloodstream. As of 1998, the most common form of blood transfusion was the intravenous transfusion of donated RBCs.[2] Typically, a healthy individual would donate 1 unit or 500 ml of "whole" blood, which would be tested for various infectious diseases, sorted by blood type, and separated into its usable components (e.g., plasma, platelets, and RBCs). This process would yield 1 unit or 250 ml of RBCs, which then would be stored until needed by a patient. [3]

While potentially lifesaving, the transfusion of donated RBCs has limitations. These include

- The need for exact blood typing and cross-matching between donor and recipient. The RBCs of each human may contain specific blood sugars, or antigens. The existence or absence of these antigens creates a complex set of allowable transfusions between donor and recipient, as shown in **Exhibit 4**. Transfusions outside of those outlined can be fatal to the recipient.

- The reduced oxygen-carrying efficiency of stored RBCs. RBCs stored for 10 days or more are only about 50% efficient at transporting oxygen in the first 8 to 12 hours after transfusion.

- The limited shelf-life for stored RBCs. RBCs can be safely stored for only about 6 weeks, after which time they are typically discarded.

- The need for refrigeration. For optimal shelf-life, RBCs must be stored at 4° Celsius (~40° F).

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[2] Historically, whole blood transfusions were the norm. Since the 1970s, however, whole blood increasingly had been separated into RBCs, platelets and plasma, allowing for (1) several patients to benefit from a single unit of donated blood and (2) a reduced likelihood of negative reaction for any given patient.

[3] In blood medicine, 1 unit is defined in terms of its therapeutic value. Therefore, "1 unit" or 250 ml of RBCs provides the oxygen-carrying capacity of "1 unit" or 500 ml of whole blood. Similarly, "1 unit" of a blood substitute (i.e., typically 125 ml) provides the same oxygen-carrying capacity of "1 unit" of RBCs or whole blood.

- The risk of disease transmission. While donated blood is tested for infectious agents, there still exists the risk of disease transmission. For example, the risk of AIDS is 1:500,000, the risk of Hepatitis B is 1:200,000, and the risk of Hepatitis C is 1:100,000.

Autologous transfusions In an attempt to overcome some of these limitations, the use of "autologous" or self-donated RBCs has become increasingly common. In an autologous RBC transfusion, a medically stable patient who anticipates the need for RBCs would have his or her own blood drawn weeks in advance, separated into its components, and saved until needed. Research has shown this process to significantly reduce a patient's rate of complication and post-operative infection, thereby hastening recovery and shortening his or her stay in the hospital.

Human Blood Supply and Demand

Human blood supply Fourteen million units of RBCs were donated by 8 million people in 1995 in the United States. Approximately 12.9 million of these units came from individuals who voluntarily donated to one of over 1,000 nonprofit blood collection organizations. By far, the largest of these organizations was the American Red Cross, which collected half of all the blood donated in the United States in 1995 through a network of 44 regional blood collection centers. Typically, the Red Cross and the other blood collection organizations supported "blood mobiles," which traveled to high schools, colleges, and places of employment to reach potential donors. The remaining 1.1 million units of RBCs were autologous donations made directly to a hospital blood center.

Increasingly, blood collection was a struggle. While 75% of all adults qualified as a donor, fewer than 5% actually donated in a given year. Historically, reasons for donating included altruism and peer pressure, while reasons for not donating included fear of needles and lack of time. Since the mid-1980s, an additional reason for not donating involved the misconception that donating put one at risk for contracting AIDS. Public education had failed to counteract this misconception.

Given the low rate of donation and the relatively short shelf-life of RBCs, it was not uncommon for medical facilities and blood banks to experience periodic shortages of RBCs. This was especially true during the winter holidays and the summer months, periods which routinely displayed both increased demand and decreased rates of donation.

Human blood demand Of the 14 million units of RBCs donated in 1995, 2.7 million were discarded due to contamination or expiration (i.e., units older than 6 weeks). Another 3.2 million units were transfused into 1.5 million patients who suffered from chronic anemia, an ongoing deficiency in the oxygen-carrying ability of the blood. The remaining 8.1 million units were transfused into 2.5 million patients who suffered from acute blood loss brought on by elective surgeries, emergency surgeries, or trauma. Exhibit 5 offers a breakdown of RBC transfusions in 1995.

In elective and emergency surgeries, RBCs were routinely transfused in situations where blood loss was greater than two units, as was typical in heart bypass and organ transplant surgeries. In surgeries with blood loss of one to two units, however, RBCs typically were not transfused in spite of their potential benefit. In these "borderline" transfusion surgeries, doctors typically avoided transfusions for fear of disease transmission or negative reaction caused by the transfused RBCs. There were approximately 1 million "borderline transfusion" surgeries in the United States each year.

RBC transfusions were also required in the approximate 500,000 trauma cases which occurred every year in the United States. These cases were characterized by the massive loss of blood due to automobile accidents, gunshot wounds, etc. However, due to the resources required to store, type, and administer RBCs, only 10% of trauma victims received RBCs "in the field" or at the site of the accident. Blood transfusions for the remaining 90% of victims were delayed until the victim arrived at a hospital emergency room. This delay was often cited as a contributing factor to the 30% fatality

rate seen in these trauma cases, as evidenced by the 20,000 trauma victims who bled to death each year prior to reaching the hospital. As one doctor put it,

> ... [T]hose first few minutes after a trauma are known as the "Golden Hour." Life and death often depends on how fast the lost blood is replaced in this period.

Looking forward, while the demand for RBCs to treat chronic anemia was expected to remain stable, the demand for RBCs to treat acute blood loss was expected to rise with the aging U.S. population. Individuals over 65 years of age comprised 15% of the adult population in 1995 and received over 40% of all "acute blood loss" transfusions. By the year 2030, this over-65 segment was expected to double in absolute numbers and to grow to 25% of the adult population.

Human blood pricing Since the AIDS crisis, it has been illegal for an individual to sell his or her blood in the United States. As such, all blood donations are unpaid. In turn, to cover their expense of collection and administration, blood collection organizations sell this donated blood to hospitals and medical centers. Once obtained, hospitals incur additional costs to store, handle, transport, screen, type, cross-match and document the blood. Estimates for these costs are outlined in Exhibit 6. Typically, these costs are passed on to the patient or to the patient's insurance provider.

The Veterinary Blood Market

The role of RBCs for animals is biologically identical to its role for humans: RBCs transport oxygen to an animal's tissues and organs. In practice, however, the availability and transfusion of blood was considerably more constrained in the veterinary market than it was in the human market.

Veterinary market structure There were approximately 15,000 small-animal veterinary practices in the United States in 1995. Of these, about 95% were "primary care" practices which provided preventative care (e.g., shots, checkups), routine treatment of illness (e.g., infections, chronic anemia), and limited emergency care (e.g., simple surgery and trauma). The remaining 5% of practices were "emergency care" or "specialty care" practices. Approximately 75% of primary care practices referred some or all of their major surgery and severe trauma cases to these emergency care practices. Across both the primary care and emergency care practices, patient volume was concentrated in dogs (~50% of patient volume) and cats (~35% of volume). Exhibit 7 provides a staffing and patient profile of small-animal veterinary clinics in the United States.

Veterinary blood demand In practice, blood transfusions in the veterinary market were infrequent. In 1995, for example, the average veterinary practice was presented with 800 dogs suffering from acute blood loss. About 30% of these dogs would have benefited significantly from a transfusion of blood, but only about 2.5% were deemed "critical cases" and received a transfusion.

The incidence of these acute blood loss cases was relatively concentrated, with 15% of veterinary practices handling 65% of all canine surgeries and 10% of practices handling 55% of all canine trauma cases. Not surprisingly, these "high incident" practices tended to be the larger primary care practices and the emergency care practices. This concentration was also evident in blood transfusions. In 1995, an average of 17 units of canine blood were transfused by each primary care practice, while an average of 150 units were transfused by each emergency care practice.

Veterinary blood supply[4] Historically, the biggest constraint to veterinary transfusions was the lack of an adequate blood supply. In contrast to the human market, there existed few animal blood

[4] Unlike the human market, transfusions in the animal market still tended to be "whole blood" transfusions.

banks. As a result, the sole source of blood for most veterinary practices were donor animals which were housed at the practice for the expressed purpose of donating blood. When a dog or cat was in need of blood, blood was drawn from a donor dog or cat and then transfused into the animal in need. For primary care practices, donor animals provided 93% of all transfused blood, while blood banks provided the remaining 7%. In emergency practices, these proportions were 78% and 22%.

About 15% of veterinary practices found the "donor animal" system to be administratively or financially prohibitive and did not offer it as a service. Of the 85% of practices that did use a donor system, few had a good sense of its cost. In particular, few practices explicitly tracked the cost of housing the donor animal or the time required to draw the blood. As a proxy for these costs, practices typically looked to the price of a unit of blood from an animal blood bank. In 1995, that cost was $50 to $100. In turn, a typical primary care practice charged a pet owner $80 to $120 per unit and a typical emergency care practice charged a pet owner $130 to $170 per unit.

Finally, most practices that conducted transfusions lacked the time and resources to properly type both the donor and recipient blood. According to one estimate, only one-tenth of practices reported always typing the blood of both the donor and recipient animal. While complications due to incompatible blood types were not nearly as severe for dogs as they are for humans, this lack of blood typing and cross-matching was shown to prolong the recovery of a patient animal.

These factors resulted in many veterinarians viewing the transfusion of animal blood as the treatment of last resort, with 84% of veterinary doctors reporting overall dissatisfaction with the blood transfusion alternatives currently available in the marketplace.

Human Blood Substitutes

Originally conceived as a vehicle to treat wounded soldiers in battlefield settings, the potential for a human blood substitute for nonmilitary use became increasingly apparent since the 1950s. This period saw a significant rise in auto accidents, the advent of open heart and organ transplant surgeries, and the AIDS crisis, which called into question the safety of the blood supply.

By 1998, several companies appeared to be on the verge of a viable blood substitute with a class of product called "hemoglobin-based blood substitutes." These products attempted to exploit the natural oxygen-carrying capabilities of hemoglobin while eliminating the limitations associated with donated RBCs. Each of these companies was attempting to (1) extract the hemoglobin found within human or animal RBCs, (2) purify that hemoglobin to eliminate infectious agents, and (3) modify the otherwise unstable free hemoglobin molecule to prevent it from breaking down. These purification and modification processes were nontrivial and represented the bulk of blood substitute research conducted over the past 20 years.

Product benefits In theory, these hemoglobin-based blood substitutes eliminated many of the limitations associated with donated RBCs. In particular, they were

- "Universal" blood substitutes, eliminating the need for blood typing and cross-matching.
- Free of infectious agents and contamination.
- Increased shelf life. These blood substitutes could be safely stored for up to 2 years.
- Immediately 100% efficient at transporting oxygen. Unlike whole RBCs, modified hemoglobin did not require a period of time to achieve peak oxygen-carrying efficiency.

In addition to these "anticipated" benefits, hemoglobin-based blood substitutes were displaying several "unanticipated" benefits which companies were only just beginning to investigate. In particular, given that hemoglobin molecules were significantly smaller than RBCs, they were able to flow to regions of the body that RBCs might not be able to reach. It was believed that this could lead to improved treatments in cases of stroke and heart attack—cases where RBCs often were slowed or restricted from reaching vital organs either due to artery blockages or decreased blood pressure.

Product shortcomings At the same time, these "hemoglobin-based" blood substitutes did have some shortcomings, including:

- A short half-life. While donated RBCs remained in the body for up to two months after transfusion, these blood substitutes were excreted from the body within 2 to 7 days.

- The potential for higher toxicity. While the human body could tolerate the limitless and continuous replacement of one's blood with donated blood, the safety of these blood substitutes had been demonstrated only up to transfusion levels of 5 to 10 units.

In spite of these shortcomings, Dr. C. Everett Koop, the former Surgeon General of the United States, proclaimed,

> When the history of 20th-century medicine is written, the development of blood substitutes will be listed among the top ten advances in medicine. … [B]ecause of its purity, efficacy and convenience, this product class has the potential to revolutionize the practice of medicine, especially in critical-care situations. … [T]he next generation will not know how tough it was for those of us in medical practice before this technology became available. [5]

Others were less optimistic. One industry analyst presented a less attractive scenario for hemoglobin-based blood substitutes:

> ... [W]e feel that there is no urgent need for blood substitutes since donated human blood is, for the most part, safe and effective. The expectation that blood substitutes will command vast markets and high price premiums is based on the assumptions that blood substitutes will prove safer and more effective than donated blood. While only time will tell if this is true, it will be an uphill battle given the widespread acceptance of donated blood.

The FDA Approval Process

Human blood substitutes fell under the strict regulation of the U.S. government's Food and Drug Administration (FDA), which required that a product be proven safe and effective for medical use before being approved for commercial release (refer back to **Exhibit 3**). By early 1998, three companies had products that were in the final stages of this process. These products differed in their source of raw hemoglobin and in the process by which that hemoglobin was purified and modified. The FDA approval process was sensitive to these differences. Short of beginning the FDA approval process anew, each company was limited in its ability to substantially alter either the source of their hemoglobin or the process by which that hemoglobin was purified and modified. In addition, given that most of the companies had patented their purification and modification processes, there was little opportunity for a new entrant to quickly gain FDA approval.

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[5] Biopure company website.

Competitors for a Human Blood Substitute

As of 1998, Baxter International and Northfield Laboratories were the only other companies in late-stage development of a hemoglobin-based blood substitute. All other competitors were either several years behind in their development of a hemoglobin-based product or were pursuing a less promising technology.

In contrast to Biopure's use of cattle as its source of hemoglobin, both Baxter and Northfield relied on human blood as their source of hemoglobin. In particular, both companies had developed a technology to extract raw hemoglobin from "outdated" human RBCs (i.e., RBCs intended for transfusion, but which had been stored for more than 6 weeks). While their production processes and their pending FDA approval did not preclude them from using fresh RBCs, it was the stated intention of both companies to initially rely on outdated human RBCs. Through 1998, Baxter had an agreement with the American Red Cross to obtain outdated RBCs at a cost of $8 per unit. Until recently, Northfield had a similar $8 per unit agreement with Blood Centers of America, another national blood collection agency. However, in early 1997, Blood Centers of America raised their price to Northfield to $26 per unit for outdated RBCs.

In addition to their reliance on human blood, the products of Baxter and Northfield also differed from Biopure's in that they needed to be frozen or refrigerated until used. Biopure's Hemopure was shelf-stable at room temperature.

Baxter International With over $5.4 billion in sales and $670 million in net income in 1996, Baxter was an acknowledged leader in the development, manufacture and sale of blood-related medical products, ranging from artificial heart valves to blood-collection equipment. In addition, Baxter had a long history of product breakthrough, having developed the first sterile blood collection device in 1939, the first commercially available artificial kidney machine in 1956, and the first Factor VIII blood-clotting factor for the treatment of hemophilia in 1966.

"HemAssist," Baxter's patented blood substitute, was expected to add to this string of breakthroughs. Representing 30 years and $250 million in effort, HemAssist was the first human blood substitute to proceed to Phase 3 clinical trials in June 1996. Initially, these trials were expected to lead to full FDA approval by late 1998. However, in October 1997, Baxter revised its estimate to late 1999 or early 2000—an announcement that was followed by a 10% dip in Baxter's stock price.

Despite this delay, Baxter recently constructed a $100 million facility with a production capacity of 1 million units of HemAssist per year. Aside from its variable cost of source material, Baxter was expected to incur production costs of approximately $50 million per year, independent of production volume. While still just industry speculation, it was anticipated that Baxter would price HemAssist between $600 and $800 per unit.

Northfield Laboratories Northfield Laboratories of Illinois also had recently entered Phase 3 trials with a hemoglobin-based blood substitute. Northfield's product, "PolyHeme," was very similar to Baxter's HemAssist in its production and usage profile. Based on early positive results from its Phase 3 trials, Northfield anticipated full FDA approval in late 1999.

In contrast to Baxter, Northfield was a small, 45-person firm that was founded in 1985 for the sole purpose of developing a human blood substitute. As such, PolyHeme represented its only product. Analysts expected PolyHeme to be priced comparably to HemAssist upon release.

By early 1998, Northfield had spent $70 million in its development of PolyHeme and in the construction of a pilot production facility with an output capacity of 10,000 units per year. While this facility was sufficient to satisfy demand during clinical trials, Northfield management recognized the need for a full-scale production facility. With this in mind, they hoped to construct a $45 million

facility with a capacity of 300,000 units per year. With this factory in place, aside from the cost of raw material, production costs were expected to be about $30 million per year, independent of production volume. By early 1998, selection of a factory site and plant construction had not yet begun.

Animal Blood Substitutes

Through early 1998, Biopure was the only company that was actively engaged in the development of a blood substitute for the small-animal veterinary market. And while there was little to prevent Baxter or Northfield (or anyone else) from attempting to enter the veterinary market, any company wishing to do so would have to initiate an FDA-approval process specific to the veterinary market. By one estimate, assuming a company immediately began such a process, it would take 2 to 5 years to bring a product to market.

Biopure and Its Blood Substitutes

Hemopure and Oxyglobin were nearly identical in terms of physical characteristics and production processes. The only difference between the two products was in the size of the hemoglobin "clusters" that were contained in the final products. In the production of Oxyglobin, both large and small clusters of hemoglobin molecules were naturally formed. However, the small clusters tended to cause minor gastrointestinal problems and discoloration of urine. While considered acceptable in the animal market, these side effects were undesirable in the human market. As a result, Hemopure followed the same production process as used to make Oxyglobin, with a final step added to remove the small hemoglobin clusters.

Biopure had a single manufacturing facility, with an output capacity varying by the production mix of Oxyglobin and Hemopure. The same equipment was used to produce either product, but only one product could be produced at a time. This resulted in an annual capacity of 300,000 units of Oxyglobin or 150,000 units of Hemopure or some linear combination inbetween. The lower output for Hemopure reflected the facts that (1) the added step to remove the small hemoglobin clusters decreased the rate of production, and (2) the removal of the small hemoglobin clusters decreased yield.

To support these levels of output, aside from the cost of raw material, Biopure anticipated overall production costs of $15 million per year, independent of volume. For raw material, it anticipated a ready supply of bovine blood priced at $1.50 per unit. Biopure paid this money to cattle slaughterhouses to collect and transport the blood of cattle that were being processed for their meat—blood that otherwise would have been discarded. It was estimated that 10,000 cattle could supply enough raw material to support full production in Biopure's existing manufacturing facility.

Status of Hemopure

As of early 1998, Hemopure was in Phase 3 clinical trials in Europe, with FDA approval for Phase 3 trials in the United States appearing imminent. In anticipation of this approval, Biopure had established sites for Phase 3 trials and was ready to proceed immediately upon approval. While acknowledging the potential pitfalls of any clinical trials, Biopure was confident that the Phase 3 trials would be successful and that the FDA would grant full approval sometime in 1999. Biopure expected to commercially release Hemopure sometime in late 1999 or early 2000.

In line with the anticipated price of Baxter's HemAssist, Biopure planned to price Hemopure at $600 to $800 per unit. However, little systematic testing had been done by Biopure to determine the acceptability of these prices. In particular, little was known of the price sensitivity of medical personnel, insurance providers, or of patients when it came to human blood substitutes.

Status of Oxyglobin

In 1997, Biopure established the Veterinary Products Division and hired Andy Wright to oversee the marketing and sale of Oxyglobin. Working under the assumption that Biopure would begin selling Oxyglobin immediately upon approval, Wright faced a host of decisions, including how to price and how to distribute Oxyglobin. Supporting him in these decisions was a team of seven employees—one director of marketing, one technical service representative (to answer technical questions and complaints), two customer service representatives (to support ordering and billing), and three sales representatives (to make sales calls and generate orders).

The pricing of Oxyglobin Some members of Wright's sales team argued for Oxyglobin to be priced at $80 to $100 per unit. These team members pointed to the price sensitivity of the vet market, arguing that few pet owners carried health insurance on their animals. They also noted that the average cost of a visit to the vet was only about $60, with few procedures costing more than $100 (see Exhibit 8). Finally, they noted that vets tended to use a simple "doubling rule" when pricing a medical product to the pet owners, bringing the end-user price of Oxyglobin to $160 to $200 per unit.

Other members of Andy Wright's sales team felt that Oxyglobin should carry a premium price of up to $200 per unit, reflecting the many advantages of Oxyglobin relative to donated animal blood. These team members pointed out that while the average cost of a visit to a primary care practice might be only $60, the cost of a visit to an emergency care practice could easily run from $200 to over $1,000. They also questioned whether veterinary doctors would just blindly double the price of Oxyglobin without regard for its high dollar contribution. Finally, they noted that at a low price, Biopure could never hope to recoup the massive cost of product development.

To better understand the channel's willingness to pay for an animal blood substitute, Biopure conducted two surveys in 1997—one survey of 285 veterinarians and another of 200 dog owners. **Table A** offers results of the veterinarian survey and **Table B** offers results of the owner survey.

In reviewing these surveys, Wright reminded himself that veterinarians often played the role of gatekeeper when it came to potential treatments, recommending less-expensive over more-expensive treatments in an effort to save their clients' money. At the same time, 90% of pet owners reported that they wanted to be made fully aware of all the alternatives available to treat their pets.

Table A Veterinarians' Reported Willingness to Trial Oxyglobin

Price to Veterinarian	% of Veterinarians Who Would Trial Product	
	Noncritical Cases	Critical Cases
$50 per unit	95%	100%
$100 per unit	70%	95%
$150 per unit	25%	80%
$200 per unit	5%	60%

Source: Biopure company records

Table B Pet Owners' Willingness to Trial Oxyglobin

Price to Pet Owner	% of Pet Owners Who Would Trial Product	
	Noncritical Cases	Critical Cases
$100 per unit	60%	90%
$200 per unit	40%	85%
$300 per unit	35%	75%
$400 per unit	30%	65%

Source: Biopure company records

The distribution of Oxyglobin Andy Wright also had to decide how best to sell and distribute Oxyglobin and how to educate veterinarians on its use. In approaching this question, he looked to the current distribution practices for medical products in the veterinary market.

In 1997, $1.2 billion worth of product was sold to veterinary practices through a network of 200 independent distributors—each of whom sold and distributed the products of many manufacturers. Two of these independent distributors were national in scope, 18 were regional (e.g., New England), and 180 were local (e.g., metropolitan Boston). **Table C** provides a sales and staffing profile for these distributors. A manufacturer might contract with one national distributor, several nonoverlapping regional distributors, and many nonoverlapping local distributors. In return for their selling and distribution efforts, a distributor would receive 20% of the manufacturer selling price on a more-established product and 30% of the selling price on a less-established or new product.

Table C Profile of Independent Distributors of Veterinary Medicines

Type of Distributor	Number	% of Total Sales	Avg. Number of Sales Reps
National	2	25%	100
Regional	18	60%	40
Local	180	15%	1.5

Source: Biopure company records

A veterinary practice could expect one 15-minute visit per week from the sales representatives of its primary distributor. These 15-minute visits would entail a focused discussion of current promotions on existing products and a more limited discussion of products new to the market. Typically, a sales rep might introduce 100 new products in a given year. To educate a particular distributor's sales reps on a new product, a manufacturer might set up a series of training sessions. These training sessions would be conducted for groups of about 10 sales representatives each and last anywhere from 1 to 4 hours, depending on the complexity of the new product.

Another $300 million worth of products were sold directly to veterinary practices through manufacturer salesforces. Termed "manufacturer direct," this type of distribution often was used by manufacturers with either high-volume, well-established products or products which required a very sophisticated sales pitch. If Biopure chose this route, in addition to the cost of maintaining a salesforce, Andy estimated the cost to physically distribute Oxyglobin to be $10 to $15 per unit.

Andy Wright also considered trade publications and trade shows as another means by which to educate veterinarians about the existence and benefits of Oxyglobin. A quick investigation revealed that five journals had almost universal coverage across veterinarians and tended to be well-read. In addition, six large veterinary trade shows held in the United States each year attracted 2,000 to 10,000 veterinarians each. Typically, these trade shows were taken seriously by attendees and were a valued source of information. Andy wondered if either of these avenues made sense for Biopure.

Biopure's Decisions

While Andy dealt with the question of how best to market Oxyglobin, Carl Rausch wrestled with the larger question of whether and when to launch Oxyglobin. Should he listen to Ted Jacobs and postpone the launch of Oxyglobin until *after* Hemopure had established itself in the marketplace? Or should he listen to Andy and immediately launch Oxyglobin and reap the near-term benefits?

Not lost on Carl was the potential impact of Oxyglobin on a possible initial public offering of Biopure stock. To this point, Biopure had remained a privately held firm with very little debt. And while they currently had no revenues, a recent round of capital venture financing had provided them with $50 million—enough money to support operations for another two years. Nevertheless, many stakeholders in Biopure were anxious to take the company public. In this regard, Carl wondered whether a veterinary product with small but steady sales might not prove more attractive to investors than a human product still under development. He was especially sensitive to this issue in light of some recent, high-profile product failures in the Massachusetts biotechnology community (see **Exhibit 9**).

With all of this in mind, as president and CEO of Biopure, Carl Rausch pondered how best to leverage the opportunity offered by Oxyglobin without jeopardizing the potential of Hemopure.

Exhibit 1 Excerpts from *The Boston Globe* Article, February 5, 1998

Biopure's Blood Substitute for Dogs OK'd

Veterinarians scrambling to find blood for badly injured dogs now have a blood substitute. Biopure Corp. of Cambridge said yesterday it received federal regulatory approval to market oxygen-carrying blood derived from the blood of cows.

Tested in over 250 dogs, the company's blood substitute, called Oxyglobin, is initially aimed at the [canine blood transfusion market], according to Andrew W. Wright, vice president of Biopure's veterinary products.

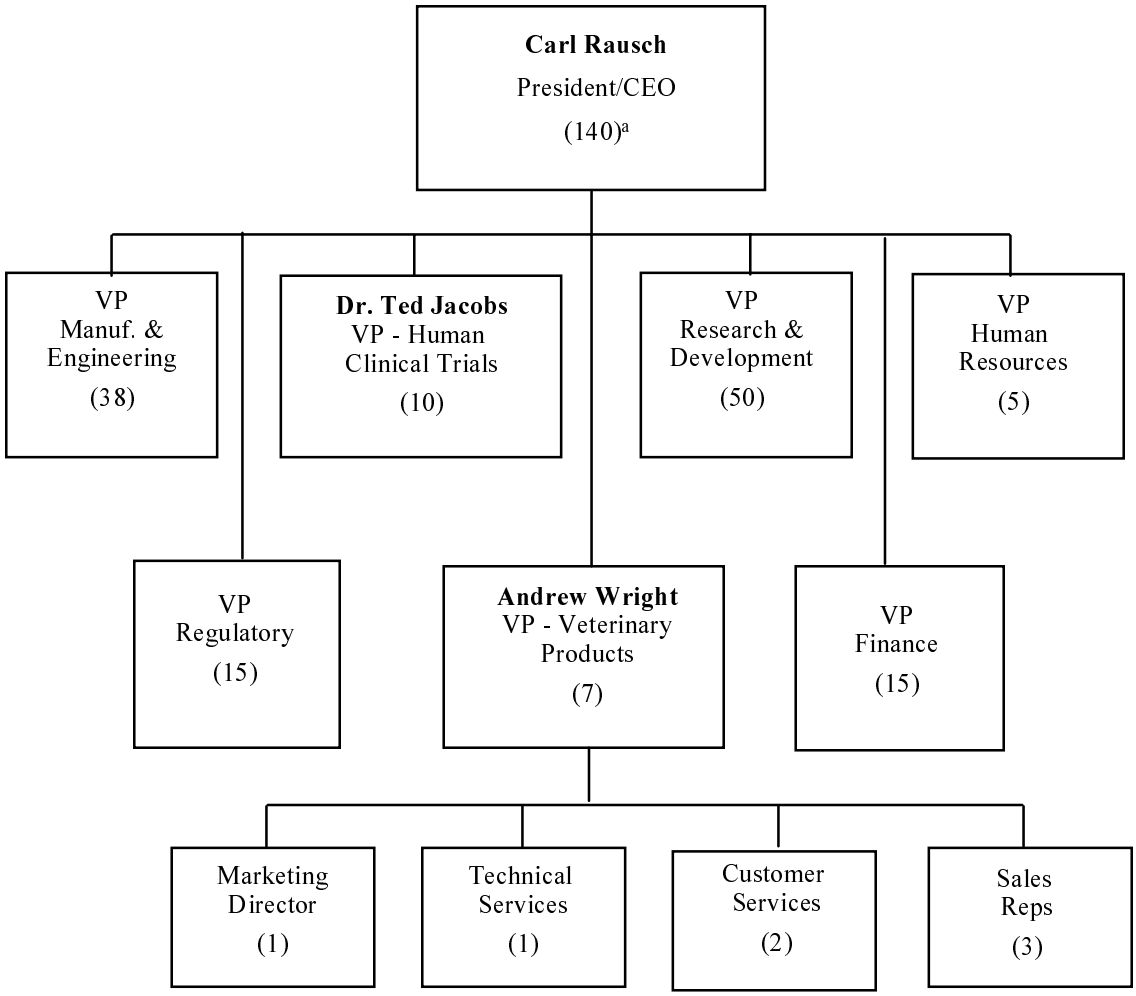
The US Food and Drug Administration approval makes Oxyglobin the first blood substitutes for dogs, designed for dogs needing blood transfusions because of blood loss from accidents, surgeries, parasite infections, or rare anemia cases.

"This is breakthrough development because it quickly gets oxygen into tissue and organs and buys time for the dog's own regenerative red blood cells to come back," said Dr. Robert Murtaugh, professor of veterinary medicine and section head for emergency and critical care services at the Tufts University School of Veterinary Medicine.

The canine version is designed to largely replace drawing blood from donor dogs some veterinarians use in emergency situations.

Unlike blood that contains red blood cells, Biopure's technology uses a highly purified bovine hemoglobin that does not require blood typing or cross-matching. [Oxyglobin] can be stored in a veterinarian's storage area at room temperature for up to two years. A single bag—equivalent to a pint of whole blood—is sufficient for small to medium-sized dogs; two bags might be needed for larger dogs.

Exhibit 2 The Organizational Structure at Biopure Corporation



Source: Biopure company records

[a] Numbers in parenthesis represents the total number of employees that fall under a particular position's span of control. Thus, 140 employees either directly or indirectly report to Carl Rausch.

Exhibit 3 The United States FDA Approval Process

Phase	Goals	Characteristics
Pre-Clinical Trials	Safety in animals	– Typical length = 5 - 10 years – Need to show safety – Hope to show efficacy – Testing animals include mice, rats, dogs, sheep, etc.
Phase 1 Clinical Trials	Safety in healthy human subjects	– Typical length = 2 - 3 years – 20 - 100 individuals – Single-site testing location
Phase 2A & 2B Clinical Trials	2A - Safety in human patients 2B - Safety & efficacy in human patients	– Typical length = 1 - 2 years – 100 - 200 individuals – Single-site or multi-site testing locations
Phase 3 Clinical Trials	Large-scale safety & efficacy In use	– Typical length = 1 - 2 years – 100 - 500 individuals – Multi-site testing locations – Double-blind testing (i.e., neither patient nor doctor aware of specific product or brand)

Source: Biopure company records

Exhibit 4 Human Blood Typing and Allowable Transfusions[a]

Donor Blood Type	% of Population	Acceptable Recipients
AB	4%	AB[b]
A	40%	A, AB
B	11%	B, AB
O[c]	45%	O, A, B, AB

Source: The American Red Cross

[a] In addition to ABO blood typing, RBCs are either Rh+ or Rh-, further complicating allowable transfusions.
[b] AB is often referred to as the "universal recipient."
[c] O is often referred to as the "universal donor."

Exhibit 5 Red Blood Cell Donations and Transfusions in the United States in 1995

Use of Red Blood Cells	Units (in 000s)
Acute Blood Loss:	
Elective Surgery:	
Anonymous Donations	5,800
Autologous Donations [a,b]	1,100
Emergency Surgery (in hospital)	1,000
Trauma (in field administration)	200
Acute Blood Loss Subtotal	**8,100**
Chronic Anemia	**3,200**
Not Transfused	
Due to Rejection	1,200
Due to Expiration	1,500
Not Transfused Subtotal	**2,700**
Total:	**14,000**

Source: Stover & Associates LLC

[a] Autologous donations are in elective surgery only. All other uses of RBCs represent anonymous donations.

[b] Autologous donations include both those units transfused and those unused units discarded.

Exhibit 6 Cost to Patient of Donated Human Blood

	Low Estimate (per Unit)	High Estimate (per Unit)
Anonymous Donations:		
Hospital Acquisition Cost	$ 75	$150
Screening/Typing/Crossmatching	25	40
Transportation/Administration	25	35
Final Price of Anonymous	**$125**	**$225**
Autologous Donations:		
Added Administration and Handling	+ 150	+ 200
Final Price of Autologous	**$275**	**$425**

Source: Stover & Associates, LLC

Exhibit 7 Profile of the 15,000 Veterinary Practices in the United States (1995)

Class of Practice	Average No. of Doctors	Relative Frequency	Average Monthly Case Load			Average Gross Revenues
			Dogs	Cats	Other	
Primary Care:						
1 Doctor Practices	1	25%	200	125	80	$265,000
2 Doctor Practices	2	30%	300	200	120	$460,000
3+ Doctor Practices	4.6	40%	450	300	160	$800,000
Average Primary Care	**2.7**	**95%**	**412**	**265**	**140**	**$570,000**
Emergency Care:						
Avg. Emergency Care	**4.0**	**5%**	**400**	**240**	**130**	**$770,000**

Source: Biopure Company Records

Exhibit 8 Small-Animal Veterinary Fees for Typical Procedures in Primary Care Practices in 1995

Procedure	Average Fee
Average Charge per Visit	***$58***
Office Call—Average Minimum Charge	$25
Boarding	$10
Hospitalization	$19
Anesthesia	$45
X-rays	$40
Blood Transfusion	$100
Hysterectomy	$80
Heartworm treatment	$250
Annual Vaccinations	$27
Rabies Vaccination	$12
Lab Tests—Average	$23
Dental Cleaning	$75
Deworming	$15

Source: *Veterinary Economics*, October, 1996, p. 45

Exhibit 9 Massachusetts Biopharmaceutical Companies' Proposed Drugs Sidelined in the 2nd Quarter, 1997

Firm/location	Date	Problem	Status of company
ImmunoGen Norwood, MA	March 18	Oncolysin B cancer drug halted after Phase 3 trial failure	Significantly downsized operations, extensive layoffs, major restructuring, sold biomanufacturing plant, and relocated corporate offices
OraVax Cambridge, MA	March 19	HNK20, a nosedrop designed to reduce hospitalization for lower respiratory infections caused by respiratory virus in infants, failed in a pivotal overseas clinical trial	Layoff of 20 people in April as part of a corporate reorganization
AutoImmune Lexington, MA	April 21	Myloral, an oral multiple sclerosis drug, did no better than placebo in Phase 3 trial	Major restructuring, now employs 20, down from 90 employees
Genzyme Cambridge, MA	May 5	Sepracoat, a surgical antiadhesion coating, was rejected by FDA advisory committee for lack of sufficient evidence of clinical effectiveness	Company selling Sepracoat in Europe; has FDA approval on related Seprafilm product
Cambridge Neuroscience Cambridge, MA	June 24	Cerestat clinical trial is halted over safety concerns by corporate partner, Boehringer Ingelheim	Six-month investigation begins to find reasons for concern

Source: *The Boston Globe*