Company: Cubist Pharmaceuticals, Inc. (CBST)
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I have evaluated Cubist Pharmaceuticals, Inc. ("Cubist" or the "Company") for its suitability as a long investment. This report highlights the merits and risks for Cubist's future.

Conclusion: Cubist is a third-tier biotechnology company likely to reach second-tier status in 2004. There is little or no risk of Cubist facing a "going concern" assessment within the next five years. With commercial success, Cubist will thrive and may well be acquired within the next ten years. Unlike most biotechnology companies, Cubist has reached the commercial stage. Cubist's first commercial product, Cubicin, was FDA approved in September and is a novel antibiotic to treat hospitalized patients with life-threatening infections. The product was launched November 4. Market adoption of this drug is certain, given the few competitive alternatives available. The breadth and velocity of this adoption are indeterminate.

Cubicin will compete directly against the current standard-of-care, vancomycin, which as a generic drug, costs one-third as much as Cubicin. However, accelerating Cubicin's adoption potential is its once-daily infusion dosing versus twice-daily for vancomycin and up to four times a day for other drugs. Cubicin's embedded cost savings in nursing time are a significant advantage. Cubicin has also demonstrated a much lower toxicity profile than its competitors and, based on laboratory data, may prove more efficacious than vancomycin against certain organisms.

Cubist's pivotal clinical trials, as with other antibiotics before it, were designed to demonstrate non-inferiority (not superiority) to vancomycin-based therapy. In order to expand the breadth of Cubicin's market potential, the Company is conducting additional clinical trials in endocarditis (a serious infection of the heart's valves) and bacteremia (infection in the blood) to expand the Cubicin label. Finally, by hiring a 75 person sales force to sell direct in the US, Cubist can realize superior operating margins. Cubist's partner, Chiron Corporation, will market in Europe. A Marketing Authorization Application, seeking European approval, is planned for submission in 2004.

In addition to vancomycin, two other products, Synercid and Zyvox, compete against Cubicin and another will come to market in 2005. Synercid has done poorly in the past three years due to its inconvenient dosing (three intravenous infusions per day) and modest efficacy. Pfizer's April 2003 acquisition of Pharmacia included Zyvox, arguably the best end-stage antibiotic available both for its convenient dosing (intravenous or oral) and broad efficacy. But, Zyvox is twice as expensive as Cubicin. Since reimbursement for nosocomial (hospital-acquired) infections are capitated, Cubicin should compete strongly.

Cubist enters the marketplace with a strong balance sheet. On October 3, the Company received $18 million from Chiron for European marketing rights. On October 16, Cubist completed a successful secondary stock offering which raised almost $85 million. At third quarter end, the Company reported $80.8 million of cash and liquid assets. Assuming a cash burn in 2004 of $90 million, Cubist will probably raise additional capital in 2004.

Analysts' 2004 sales estimates for Cubicin range from $40 to $80 million ($55 million consensus) rising to ≈$250 million in 2007. Wall Street's estimates are historically optimistic while the treatment of end-stage infectious disease is notoriously unpredictable. Still, if Cubist posts first year sales of $30 million, the drug will be considered a success. For comparison, Pfizer's Zyvox has been on the market for three years but is expected to only reach $200 million this year. Lilly's Vancocin® vancomycin, <u>the</u> gold standard, had sales of $217-, $205- and $211 million in 1999, 2000 and 2001, respectively after more than 30 years on the market. Departing the infectious disease market, Lilly discontinued Vancocin's manufacture in 2002. Finally, for comparison with past analyst projections, in September 2000, Deutsche Bank projected Aventis' Synercid to reach 2003 sales of $280 million. Synercid did $28 million in 2002 and was sold to King Pharmaceuticals last December.

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Company Background

Founded in May 1992, Cubist Pharmaceuticals Inc. ("Cubist" or the "Company") is based in Lexington, Massachusetts and is surrounded by literally hundreds of biotechnology companies in and around Boston. Cubist develops *antibiotics* to treat serious infections, i.e., those affecting patients who are hospitalized and typically require intravenous (IV) therapy. The Company planned to rationally design drugs that could specifically block protein synthesis in bacteria without affecting protein synthesis in a person's cells. Early on, this research platform was supported with funding from Pfizer, Bristol-Myers and Merck. Cubist continues its in-house R&D efforts, but has leveraged its skill-base with an active drug in-licensing capability.

In October 1996, the Company completed a distressed IPO, issuing 2.5 million shares at $6.00 per share ($38 million pre-money), well below the intended price range of $10 to $12 per share. Investment banks included UBS Securities, Hambrecht and Quist, and Pacific Growth Equities.

In April 2000, Cubist raised over $80 million in gross proceeds from a secondary offering of 2.5 million shares at $33.00 per share. The syndicate included Robertson Stephens, Pacific Growth Equities, H&Q, ING Barings and Lazard Frères.

In October 2001, Cubist issued $125 million of 7-year, 5.5 percent debt convertible into common shares at $47.20.

Finally, this past mid-October, the Company completed a secondary offering of 7.45 million shares priced at $10.50. Its bankers included Morgan Stanley, Pacific Growth Equities, WR Hambrecht and Nesbitt Gerard.

It is worth noting that, while the public equity market "sieve" may expand and contract, Cubist has also been able to raise over $90 million, as a public company, in the private placement market. This figure does not include $165 million raised as convertible securities.

Cubicin

By 1997 Cubist's management recognized the difficulty underlying rational drug design and (wisely) licensed a novel antibiotic, daptomycin, from Eli Lilly in November. In the late 1950's, Lilly had developed vancomycin (Vancocin®), which until the late 1990's, was the most powerful antibiotic available. Daptomycin was one of hundreds of compounds discovered by conventional screening ("spray and pray") against vancomycin-resistant bacteria. During daptomycin's clinical development, begun in 1988, Lilly observed skeletal muscle complications in some patients and dropped the program in 1991. Based on animal model studies, Cubist determined that these complications were related to the three-times-per-day dosing schedule as opposed to the peak plasma concentration of drug. Cubist trade named daptomycin Cidecin, then Cubicin and began the antibiotic's pivotal clinical development in early 1999.

On September 12, the FDA cleared Cubicin as an IV antibiotic to treat complicated (meaning "for use in hospitalized patients") skin and skin structures (cSSS), due to gram positive bacteria. As detailed below, these infections are typically life-threatening and include major abscesses, traumatic wounds and diabetic ulcers. In addition, a large percentage of these infections are acquired within the hospital setting where antibiotic-resistant organisms are abundant. For example, Cubicin is indicated for the roughly 600,000 people in the US who contract methicillin-resistant S. aureus (*MRSA*) cSSS infections each year. *For the rest of this decade, Cubist's value will lie squarely on Cubicin's commercial success. This report focuses on Cubicin's market opportunity and relative competitive profile.*

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CAB-175

In August 2002, Cubist licensed its second antibiotic, CAB-175, from Novartis' generic drug unit called Biochemie GmbH (renamed Sandoz in March 2003). The Sandoz generics unit manufactures almost 50 antibiotics from over half-a-dozen chemical classes. This molecule is a novel, chemically modified cephalosporin which, in test tube studies, has proven bacteriocidal against certain antibiotic-resistant bacteria. Other cephalosporins (like Roche's Rocephin) are inactive against these particular bacteria. Safety testing in healthy volunteers began in June 2003. *Given the early stage of clinical testing, there is no financial value assignable to this drug over the next ten years.*

Oral Rocephin

In November 2000, Cubist licensed a (potentially) oral formulation of Roche's Rocephin (ceftriaxone). FDA approved in late 1984, Rocephin is a third-generation cephalosporin antibiotic which has only been available as an IV agent. A generic version (developed by India-based Lupin) of the IV drug was approved this past September 30 with a US market launch planned after Rocephin's patent expires in July 2005. Early human testing of the oral Rocephin formulation has begun. The availability of oral Rocephin would clearly facilitate patient "step-down" from the IV drug. However, with 2002 sales of more than $1 billion in 2002 and a generic version already approved, the economic impact of oral ceftriaxone on Cubist's future may be limited. *There is no financial value assignable to the oral Rocephin project over the next five years. Should the formulation prove successful, it may be worth $100 million*[1] *per year over the next five-to-ten years.*

Introduction to Antibiotics

Second only to improved sanitation (chlorinated drinking water, sewer systems) which added 20 years, antibiotics have increased Americans' life span (by ten years), from 47 in 1900 to 77 today. Discovered in 1928, but only widely available by 1945 (no prescription was required), penicillin was the first true antibiotic. Initially effective against what is still one of the most irrepressible bacteria, Staphylococcus aureus (S. aureus), penicillin resistant strains of S. aureus were documented only two years after its market introduction. For the past 60 years, clinical researchers have played a game of biochemical leapfrog developing new antibiotics to fight resistant bacteria, only to discover newly resistant strains after several years of antibiotic use. This game has no end, enabling a market opportunity in perpetuity.

Thus, over the same period, roughly 180 variations of perhaps 18 molecular classes of antibiotics have been commercialized. And yet in 2002, 80 percent of all antibiotic prescriptions in the US were for five drugs (GlaxoSmithkline's Augmentin, Pfizer's Zithromax, Bayer's Cipro, Abbott's Biaxin and Johnson & Johnson's Floxin). The worldwide market for antibiotics (excluding antivirals) was $21.2 billion. The largest antibiotic categories are for those drugs widely prescribed by general practitioners. These include the quinolones ($3.5 billion in 2002, includes Cipro and Floxin), the penicillins ($3.7 billion in 2002, includes Augmentin) and the cephalosporins ($3.7 billion in 2002, mostly generics). It is this concentrated use, poor patient compliance (prescription stopped early) and inappropriate prescriptions (e.g., antibiotics can not treat viral infections) that have helped fuel the rise of resistant organisms.

In recent years, the succession of antibiotic use, especially in the hospital, has been:

(1) Try to use a *penicillin*, a *cephalosporin* or one of either drug's many derivatives. Other arrows in the antibiotic quiver include the *quinolone* and *macrolide* classes. If these are unsuccessful at fighting the infection, which is often known within 48-72 hours, and especially to treat S. aureus or Enterococcus infections, then

[1] This assumes that the oral formulation commands 50 percent of the dollar share of the Rocephin market which is expected to quickly decline to 20 percent of its current size once the generic (IV) drug is launched in 2005.

(2) begin *methicillin* therapy, historically the penultimate drug of choice. When possible, the bacteria causing an infection are isolated and tested in the laboratory against a battery of antibiotics. With the alarming increase in MRSA, more powerful antibiotics have been developed. Until recently, the last drug in the clinician's armamentarium, and most toxic antibiotic, had been

(3) *vancomycin*. During the 1970s and early 1980's, it was believed that due to vancomycin's dual modes of action, resistance would not develop. In 1987, the first vancomycin-resistant enterococcus (*VRE*) in the US was documented. While microbiologically benign (the bacterium lives in a symbiotic relationship in the human gut), an infection in the bloodstream can be dangerous. Also, the observation of enterococci resistant to vancomycin presaged vancomycin resistance in more ominous organisms[2]. In July 2002, the first vancomycin-resistant S. aureus (*VRSA*) in the US was reported. Its resistance was due to a gene originating in VRE. Fortunately, two powerful new antibiotics had already received FDA approval, Aventis' Synercid (September 1999) and Pharmacia's Zyvox (April 2000), both of which were effective against VRSA.

Antibiotic Clinical Trials

Most drugs are discovered by testing in animal models of disease. For example, obese, diabetic or hypertensive (high blood pressure) rats are commercially available. New antibiotics, however, are discovered by screening compounds or extracts against hundreds of different bacterial strains, each in pure culture (*in vitro*). Further testing is performed in laboratory animals (*in vivo*), each infected with one relevant bacterial strain. However, once clinical trials begin, other than restricting patient enrollment by the site of infection (lungs, gastrointestinal or urinary tract, skin, blood), investigators "take what they get." This means that most new antibiotics, especially for severe infection, are approved for a limited (what was actually tested) number of infections. To help physicians, the prescribing guidelines always contain *in vitro* data with the caveat that "...their clinical significance is unknown." Finally and perhaps most importantly, pivotal clinical studies are never "placebo controlled." That is, no patient is ever treated with a dummy pill. All studies compare the test drug against standard-of-care comparator drugs. Typically, these studies therefore, are designed to demonstrate non-inferiority (efficacy within ten percent of the comparator group) rather than superiority to the comparator treatment. Thus, in describing the results from a typical clinical trial, companies break down the patient population into as many as four groups, as described below, using Cubist's US pivotal trial as an example.

(1) Overall success, defined as clinical resolution with no further antibiotic therapy required. Typically, this includes every enrolled patient who was treated with at least one dose, the so-called intent-to-treat (ITT) population. For example, Cubist's US pivotal trial had 256 patients treated with Cubicin on an ITT basis. This is the most rigorous analysis.

(2) m-ITT, is a modified ITT population representing those who, upon enrollment, tested positive for the intended subgroup of bacteria. In Cubist's trial, 209 patients treated with Cubicin had a gram-positive infection at entry and, thus, were included in the m-ITT cohort.

(3) Clinically evaluable defines the patient cohort which, from beginning to end, met all prospectively defined criteria for the trial. Factors include inclusionary/exclusionary criteria, duration of therapy and all called-for evaluations. Of the 256 patients enrolled, 223 treated with Cubicin qualified for inclusion in the CE cohort.

(4) Microbiologically evaluable further refines the analysis by evaluating patients common to (2) and (3) above. Seventy-three percent (187) of the 256 patients enrolled and treated with Cubicin were included in the ME analysis.

In reporting the results from the US study described above, Cubist provided the information reproduced in Table 1 on the following page.

[2] Resistance can be intrinsic to an organism or acquired through the transfer of genetic information; e.g., the vanA or vanB genes, conferring resistance to vancomycin, are transferrable between bacteria.

Table 1: Clinical Success Rates for CIDECIN vs. Comparator in Study 9801

	CIDECIN		Comparator		95% Confidence
	Total	Success	Total	Success	Interval*
ITT	256	167 (65%)	261	166 (64%)	-9.9, 6.6
MITT	209	140 (67%)	212	142 (67%)	-9.0, 9.0
CE	223	167 (75%)	222	166 (75%)	-8.2, 8.0
ME	187	140 (75%)	189	142 (75%)	-8.5, 9.0

* Statistical equivalence defined as ± 10 percent.
Source: Cubist Pharmaceuticals press release, October 26, 2001

It is clear from the table above that Cubicin is no worse and thus, comparable to, the standard-of-care drugs used in the comparator arm. For example, 65 percent of the ITT population treated with Cubicin resulted in clinical success as compared with a 64 percent success rate using the comparator drug. In this, and a very similar clinical trial conducted outside of the US, the comparator drugs included vancomycin or a semi-synthetic penicillin such as oxacillin or nafcillin. Individual clinicians were free to choose the comparator drug they thought best. Both Zyvox and Synercid were tested in similarly designed clinical trials. Thus, with Cubicin and vancomycin (now generic), four drugs compete for the hospital-based, serious infection market. These four drugs are compared on the following page.

There are two important differences, affecting potential market size, between most new drugs and specialty antibiotics such as Cubicin. First, the top ten drugs, by sales, reach that status by virtue of their chronic use and a growing patient population. For example, the top selling drug worldwide is Pfizer's Lipitor, expected to top $9 billion this year. Used to lower cholesterol, it does not cure hypercholesterolemia. In fact, in 2002, none of the top ten drugs sold in the US cured their respective disease. Once started on the drug, patients stay on the drug indefinitely as new patients join the cohort. Likewise, drugs for high blood pressure and diabetes are used chronically by expanding patient populations. Antibiotics like Cubicin are used acutely, usually for less than two weeks, until the patient is cured. As hospitals get better at preventing serious infections, annual antibiotic use could actually *decrease*. This is unlikely, due to a second issue, that of antibiotic resistance. Since bacteria inevitably become resistant to antibiotics and the prevalence of these bacteria increases with broader antibiotic use, clinicians try to restrict the use of their best antibiotics until absolutely necessary. Doctors save the best for last. Paradoxically, if Cubicin's clinical utility were to expand, its sales could conceivably decrease. Thus, hospital-based infectious disease specialists face a constant dilemma. These physicians must balance the clinical efficacy (i.e., a patient benefit) of an antibiotic with the inherent risk of ultimately inducing resistance (i.e., a population disservice) to that antibiotic by virtue of excessive use. In addition, economic considerations necessarily underlie clinical practice.

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Overview

Drug (Source)	Approval Date	Listed Bacteria	Dosing Schedule	Diseases, Patient Population
Cubicin (Cubist)	Sept/2003	*'Cidal* for MRSA, 3 strains streptococcus, vancomycin-sensitive E. faecalis	30-minute, once/day *IV* (arm) at 4mg/Kg for 7-14 days.	cSSS in patients > 18 years old.
Vancomycin (Lilly, generic)	1958	*'Cidal* for MRSA, E. faecalis	1-2 hour, twice/day *IV* (arm) at 15mg/Kg until clinical success.	cSSS, endocarditis, bacteremia in all age groups.
Zyvox (Pfizer/Pharmacia)	Apr/2000	*'static* for MRSA, vancomycin-resistant E. faecium, *'cidal for* penicillin-sensitive streptococcus pneumoniae, 2 other strains of streptococcus.	1-hour IV, twice/day *or oral* at 600mg for 7-28 days.	cSSS, bacteremia, nosocomial neumonia in all age groups.
Synercid (King)	Sept/1999	*'cidal* for vancomycin-resistant E. faecium, *'static* for vancomycin-resistant E. faecalis.	1-hour, thrice/day for VRE, twice/day for methicillin-sensitive S. aureus, *IV* (CVC) at 7.5mg/Kg for > 7 days.	cSSS, bacteremia in patients > 16 years old.

Market Adoptability

Drug (Source)	Drug Cost	Cost per Course-of-therapy	Storage	Side Effects	Comments
Cubicin (Cubist)	$150/500mg vial	70 Kg patient for 7 days (1,860mg) costs *$600*.	Refrigerated	De minimis	Once per week test for skeletal muscle damage recommended.
Vancomycin (Lilly, generic)	$7.03/500mg	70 Kg patient for 7 days (≈ 15 grams) costs *$210*.	Refrigerated	Kidney, hearing, blood cell counts impairment are rare.	Sixty percent of nosocomial S. aureus infections are methicillin-resistant.
Zyvox (Pfizer via Pharmacia)	$36.80/200mg	At $220/day, 7 days cost *$1,546*.	Room temperature	Suppresses bone marrow activity; Blood cell count monitoring.	Only drug not dosed by weight; Oral and IV formulation equally effective.
Synercid (King via Aventis)	$114.58/500mg	$245-$375 per day, 7 days cost *$1,700-$2,600*.	Refrigerated	Serious venous irritation at injection site.	Eighty percent of nosocomial Enterococcus infections are E. faecalis, not E. faecium.

Source: For both tables, Prescribing Information Product Inserts, Companies' SEC reports, Medicare's HCPCS Drug Pricing Coding System File (Oct. '03), Morgan Stanley, Legg Mason, First Albany, Deutsche Bank, SG Cowen.

Competitive Analysis

For the present, Cubicin is at a cost disadvantage to vancomycin while providing no clinical benefit; but that analysis is incomplete. First, intravenous dosing requires "nurse time" and Cubicin's once-a-day dosing could play a significant role in its adoption. Pharmacy and Professional Services represent very different line items in a hospital's cost structure. Thus, no tangible cost savings would accrue from reducing infusion duties by half, since other duties would replace the time savings; no nurses would be fired. Still, time remains an inflexible, highly-valued asset in the hospital. Second, as a novel molecular entity with a unique mode of bacteriocidal action, Cubicin provides a genuine addition to an armamentarium that is not expanding rapidly. With more rapid and broader adoption of in-hospital screening for drug-resistant organisms coupled with their growing prevalence, clinicians may find themselves with few options. Finally, in both pivotal clinical trials, roughly twice as many patients receiving Cubicin were clinical successes in four-to-seven days as those receiving the comparator drugs -- Cubicin was faster acting. This observation was made as a retrospective analysis of the data, and so could not be included in Cubicin's Package Insert. Some analysts have interpreted this result as having the potential to shorten LOS (length-of-stay) in the hospital, but that benefit remains to be proven.

Cubist is pursuing a broader label by conducting clinical trials in patients with endocarditis (a serious infection of the heart's valves) and bacteremia (infection in the blood). Data from these trials should be available in 2004. If successful, label expansion would be likely in 2005. Unfortunately, an earlier study of Cubicin in pneumonia failed and a warning against its use in that indication also appears on the label. Still, the risk of additional contraindications is well worth the opportunity for a broader label.

The need to test patients receiving Cubicin for skeletal muscle damage (not smooth or cardiac muscle) harks back to early clinical studies performed with more frequent dosing. In fact, there was no evidence of skeletal muscle damage in either of Cubist's pivotal clinical trials and none seems likely to emerge. However, prudent clinical practice with a new drug demands monitoring for adverse events, and this added testing will inhibit early, widespread adoption. With increased experience, testing for skeletal muscle damage is likely to fade, except for certain, high risk patients.

Cubicin offers at least one significant advantage over Synercid. While both must be delivered intravenously (and neither has an oral formulation), Synercid's well-documented irritation of the smaller arm veins means that for cSSS patients, drug delivery is likely to require a *CVC* (central venous catheter) or *PICC* (peripherally-inserted central catheter) line. Essentially, both catheters reduce venous irritation by delivering the drug into the larger superior vena cava where the drug is quickly diluted. Simply put, Synercid requires a more complex delivery system than Cubicin. A second potential issue is that, unlike Cubicin which received full FDA approval, Synercid was cleared for its single indication under FDA's "accelerated" approval program. This means that Synercid's approval was based on a surrogate endpoint (clearance of bacteremia), not a clinical endpoint (cure of the underlying infection). Furthermore, an accelerated approval is conditional, dependent on subsequent trial(s) demonstrating clinical value. This regulatory cloud hanging over Synercid's future remains unresolved.

Vancomycin's dual advantages over Cubicin are cost and a long history of use. While not inexpensive, Zyvox has other advantages over Cubicin. These include a broader label (including pneumonia, for example), easy storage at room temperature, and oral availability. The ability of a hospital to discharge a patient while still on antibiotic therapy is significant. One advantage Cubicin has over Zyvox is that Cubicin is *bacteriocidal*, where Zyvox is *bacteriostatic*, against MRSA. For this important indication, especially in those patients with weakened immune systems, Cubicin is the better drug. As noted above, with 60 percent of nosocomial S. aureus infections showing methicillin resistance, Cubicin clearly has the potential to overshadow Zyvox for certain uses.

With the market for end-stage antibiotics constrained as discussed above, several large pharmaceutical companies have abandoned this sub-sector of infectious disease. Roche explicitly exited the field in 1999, Lilly in 2001 and Aventis in 2002. This has created an in-licensing opportunity for smaller specialty pharmaceutical companies, where product sales of $100 million per year make economic sense. One such company is Intermune, Inc. In October 2001, Intermune licensed oritavancin, a chemically-modified version of vancomycin (which is a natural product). Intermune has completed

two, pivotal clinical trials in cSSS and has demonstrated non-inferiority to a vancomycin-based drug regimen. An NDA submission is planned for the second quarter 2004. Assuming FDA approval, the drug could be on the market in the spring of 2005. Although oritavancin has a much longer circulating half-life than vancomycin (facilitating its once daily dosing), it is no more potent against MRSA than vancomycin.

One other drug worth noting is Aventis's Targocid (teicoplanin) which is also related to vancomycin. Although approved in the UK in August 1989, it has never been submitted for FDA review and, therefore is not available in the US. Given the absence of a US-based regulatory effort and a US patent issued in 1976, teicoplanin is not a foreseeable market threat to Cubicin.

Manufacturing

Despite its September 12 approval from the FDA, Cubicin was commercially launched only very recently. The drug is a natural product produced by and purified from Streptomyces roseosporus. For Cubist's clinical trials, the active drug substance was manufactured by ACS Dobfar SpA, a 30 year-old, privately held contract manufacturer (mostly cephalosporin antibiotics) based in Milan, Italy. However, ACS's facility has not received FDA approval for commercial manufacturing. ACS does not currently provide any commercial drug substances to publicly traded US companies for sale in the US. Cubist does not expect ACS to have FDA approval until the end of 2004, but that approval is not at all certain. Until then, Cubicin's commercial manufacturing resides with a single supplier, DSM Capua, an Italian-based facility that is a unit of DSM N.V., based in The Netherlands. DSM is the world's largest manufacturer of so-called active pharmaceutical ingredients (API) and also manufactures King's Synercid antibiotic. After an API is manufactured and purified to bulk drug substance, it is then packaged in what is called the final-fill-and-finish (FF&F) step; for Cubicin, FF&F has been contracted with Abbott Laboratories which has a long history of success.

On its November 5, 2003 third quarter conference call, Cubist noted that a second, unnamed, manufacturer should come on line in mid-2004. While providing the assurance of drug supply, in fact, DSM already has current capacity to produce 600,000 doses of Cubicin, worth roughly $55 million in product sales.

Sales and Marketing

Cubist has hired a 75-person sales force and will sell direct in the US. On its November 5, 2003 third quarter conference call, Cubist indicated that its domestic marketing plan will be directed at getting infectious disease specialists to prescribe Cubicin ahead of vancomycin. The strategy is wise for two reasons. First, laboratory testing suggests that Cubicin will be more efficacious than vancomycin against certain organisms. Using Cubicin earlier avoids the genuine risk to a very sick patient of what amounts to "delayed treatment." Second, targeting vancomycin-resistant patients (i.e., patients who have failed vancomycin therapy) would result in a much smaller market opportunity, possibly forcing Cubicin, unnecessarily, into a drug-of-last-resort niche.

In January 2001, Cubist had signed an agreement with Gilead (which has a strong antiviral franchise) to sell Cubicin, if approved, in Europe. Cubist received $13 million up-front. By September 2002, Gilead had decided that the market opportunity was too small and terminated the agreement. On October 3 of this year, the Company announced a similar partnership with Chiron Corporation. Despite the up-front payments of $8 million in cash and $10 million in Cubist equity, the announcement was met with little excitement. Chiron has neither a strong franchise in antibiotics or in hospital-based European markets. Specifically, Chiron sells tobramycin (Tobi), an inhalational antibiotic indicated solely for cystic fibrosis patients with Pseudomonas aeruginosa infections. Chiron also markets interleukin-2 (Proleukin), which is used to treat two types of cancer, renal cell carcinoma and melanoma. Neither drug puts Chiron's sales reps in front of hospital-based infectious disease specialists. Finally, the Chiron transaction included an additional $32 million in milestones.

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Cubist's plans for Europe are for a regulatory submission in 2004. This filing is called a Marketing Authorization Application (MAA) and is analogous to an NDA filing in the US. If a panel of experts, the Committee for Proprietary Medicinal Products (CPMP) is required to review the MAA, and a "positive opinion" is issued, then the European Medicines Evaluation Agency (EMEA, like the FDA) has 90 days to ratify the CPMP opinion and grant the MAA. From beginning to end, with no stoppages, this process takes about 300 days, usually longer. Cubist expects European approval in 2005.

Financial Overview
(CBST - NASDAQ)

Recent Price[1]	$11.76	Market Cap ($ Million)	470
52-week Range	$5.53 - $14.75		
Shares Outstanding[1,2]	40.0 million	Cash/Share[1,2]	$4.59
Institutional Ownership (June '03)	≈ 95 percent	Technology value/share	$7.17
Shares in Float	38.4 (96 percent)	Analysts:	3 Buy, 1 Hold
Average daily volume (90-day)	759,000	Needham, WR Hambrecht, First Albany, Legg Mason	
Shares short (Oct.)/Short ratio (days)	4.09 million/5.4	Technology value/LTM Revenues:	N.A.
LTM Revenues ($ Million)	11.5	P/E	N.A.
FY'02A EPS	($2.49)	Fiscal Year End	December
FY'03E EPS[1,2]	($2.74)	Founded	May 1992
IPO price/date	$6.00/October 1996		Since:
		Pres/CEO: Michael Bonney	January 2002
		CFO: David McGirr	November 2002
		COB: Scott Rocklage, PhD[3]	March 2000

[1] *Source: Cubist SEC filings, Multex at November 6, 2003*
[2] *Includes shares and proceeds from October 2003 public offering.*
[3] *Dr. Rocklage served as President/CEO from July 1994 to March 2001.*

Financial Snapshot
($ million)

9/30/03	9/30/02	2002	2001	
Cash, ST, LT Investments	80.8	171	151	243
LT Debt	208	209	208	209
Revenues (R&D, no product)	0	5.8	11.5	14.4
R&D Expense	11.9	14.6	55.9	63.7
S&M Expense[4]	5.8	N.A.	N.A.	N.A.
(S)G&A Expense	13.1	5.7	29.1	21.8
Net Loss	(34.2)	(17.0)	(82.4)	(69.9)

[4] From inception, SG&A expenses were consolidated until FQ3 2003, when, upon Cubicin's commercialization, Cubist began reporting S&M as a separate line item.

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With roughly 200 employees, Cubist appears somewhat top-heavy for a company just beginning to sell its first product. In addition to its top three executives, Cubist also sports three Executive-, three Senior- and eight Vice Presidents. For comparison, 25 year old Biogen, with 2,600 employees, $1.2 billion in annual revenues and a market capitalization of over $5 billion has five Executive Vice Presidents.

Since inception, the Company has recorded $256 million of paid-in capital and, at June 30, 2003, had an accumulated deficit of $310 million. On October 21, Cubist completed a public offering of 8.57 million newly issued shares at $10.50 per share (net $84.6 million). Many publicly traded biotechnology companies have spent far more dollars, over many more years and still have no drugs on the market. By any measure, Cubist is a rare success story with a genuine commercial opportunity at the door.

Investment Merits:

- Commercial Opportunity Cubist has succeeded where most biotechnology companies have not. It identified a viable product (abandoned by its discoverer), designed a clinical development program and successfully navigated an FDA approval. While new hurdles lie ahead, President and CEO Michael Bonney brings the proper perspective of Sales and Marketing to what has been historically viewed (based on its former CEO's persona) as an R&D boutique. If Cubicin can demonstrate even modest commercial success -- the Company should guide Wall Street's expectations lower, but it may be too late for that -- Cubist's future will be most secure.

- Good visibility Cubist has solid coverage on Wall Street. Small biotechnology companies need to trumpet their progress (at the price of also announcing their stumbles) in order to command some "signal above the noise." Timely reporting of news by sell-side analysts will keep investors apprised of Cubist's progress, typically with an optimistic bias. The recent secondary offering should have "greased the skids" for continued, upbeat investment bank coverage.

- Acquisition Candidate The great biotechnology consolidation has been "imminent" for over 15 years. Still, Big Biotechs have become increasingly aggressive, and equally important, smaller companies more accepting, of mergers. Examples include Gilead's acquisition of Triangle Pharmaceuticals, Millennium's acquisition of Cor Therapeutics and Cephalon's acquisition of CIMA Laboratories, among others. The ideal target has product(s) and pipeline.

  Cubist's European marketing partner, Chiron, is perhaps the most acquisitive biotechnology company ever. Beginning with its first acquisition of Cetus Corporation (1991, biologicals), Chiron has acquired Viagene (1995, gene therapy), Hoechst Behringwerke's human vaccine unit (1996), Pathogenesis (2000, pulmonary antibiotic), Matrix Pharmaceuticals (2002, oncology) and, this past summer, Powderject Pharmaceuticals (vaccines), among others. Should Cubicin prove successful, an acquisition of Cubist by Chiron would not be surprising.

Investment Risks:

- Market Adoption The market for end-stage antibiotics will never vanish. Conversely, it will never reach blockbuster (> $500 million per year) status. Product-specific features such as ease-of-use, clinical utility, specificity, toxicity, drug-drug interactions and of course, cost are all part of a product's market gestalt. And yet, there is the old Wall Street adage that "drugs are sold, not bought." Cubist's new sales force will compete against low-cost, generic vancomycin *and* Pfizer, arguably the most aggressive sales force in the US, promoting Zyvox. As conservative as infectious disease intensivists are, they also recognize the limited armamentarium at their disposal and, therefore see the value of gaining experience with a new drug. In one very real sense, Cubicin's real world clinical trials began the day the drug was launched. Cubist has indicated that it will employ "drop ship" drug distribution (no wholesaler inventories), so there will be no "buffer" against weekly usage variation. Therefore, there should be reasonably accurate visibility on market adoption after the first full quarter of sales.

- Capital Resources Cubist's balance sheet is adequate, but will need strengthening in 2004. The Company has provided no guidance on cost-of-goods, manufacturing efficiency/capacity and related product costs. Also, Cubist will need to pursue label expansion (more disease indications) by running additional clinical trials. The sales force is on board and the product has launched. If Cubist can report broad-based, recurring (albeit low, absolute) sales results, the Company should have no difficulty raising at least an additional $90 million in 2004 (its projected cash burn). If not, the Company will need to rationalize its R&D and clinical development efforts.