# EXHIBIT 16

BERNSTEIN RESEARCH CALL

October 15, 2003

**Catherine J. Arnold** • arnoldcj@bernstein.com • +1-212-756-1885
**Geoffrey Porges** • porgesgc@bernstein.com • +1-212-823-2910
**Gbola Amusa, MD, CFA** • amusagb@bernstein.com • +1-212-823-2881

# Roche & Amgen: Taking CERA Seriously

| Ticker | Rating | CUR | 10/14/2003 Closing Price | Target Price | YTD Rel. Perf. | EPS 2002A | EPS 2003E | EPS 2004E | P/E 2002A | P/E 2003E | P/E 2004E | Yield |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ROG.VX | O | CHF | 110.75 | 138.00 | 3.6% | 5.09 | 4.52 | 5.84 | 21.8 | 24.5 | 19.0 | 1.3% |
| AMGN | M | USD | 67.14 | 66.00 | 18.3% | 1.39 | 1.92 | 2.35 | 48.3 | 35.0 | 28.6 | 0.0% |
| SPX | | | 1045.35 | | | 47.95 | 52.75 | 55.50 | 21.8 | 19.8 | 18.8 | 1.6% |
| MSDLE15 | | | 924.61 | | | 35.22 | 49.45 | 58.26 | 26.3 | 18.7 | 15.9 | 3.2% |

O – Outperform, M – Market-Perform, U – Underperform

## Highlights

- Roche has alerted the medical and biopharmaceutical world that it is aiming to increase its stake in the over $9 bn global market for erythropoietins by launching a product known as CERA (continuous erythropoiesis receptor agonist).
- CERA appears to be a substitute in many ways to Aranesp, Amgen's second generation erythropoietin launched in 2001. Aranesp sales were $416 mm in 2002, and we forecast worldwide sales of $3.7 bn in 2008.
- **We believe that there are three key issues that will determine CERA's potential and its relative threat in the lucrative U.S. market: its clinical profile, the ability of Roche to break Amgen/J&J's patent defenses in the U.S., and its competitiveness against erythropoietin generics.**
- Our latest analysis of these three dynamics support **our hypothesis that CERA's chances of entering the U.S. market are good – a view not fully appreciated by consensus.**
- In the U.S., our proprietary patent analysis, review of publications and opinion leader interviews confirm that CERA should meet or exceed Aranesp's current 1-2 week dosing interval and may achieve every-three-week or every-four-week dosing, sufficient for once-per-chemotherapy-cycle dosing. The current safety profile of CERA, including immunogenicity, after studies involving hundreds of patients, is clean.
- **Roche's issued patents for CERA suggest that meaningful differences exist between CERA and native human erythropoietin, and between CERA and Aranesp, and that CERA should enter both U.S. and E.U. markets in 2007.**
  - We expect the U.S. erythropoietin market, currently shared by Amgen and Johnson & Johnson, to achieve $6.6 bn in 2003 sales, with 9.3% compound annual growth expected to drive the market to a $10.3bn potential in 2008.
  - We expect one or more discounted generic versions of human erythropoietin to be introduced in Europe in 2005. As a result, the market will grow more slowly, and the opportunity for Aranesp and CERA will be limited.

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

- We believe true generic entry will not occur in biopharmaceutical markets. Increased barriers to entry arise since individual product, process and plant approvals are inseparable from clinical data supporting each product's approval. Nevertheless, stakes are high and competitors are actively developing direct and modified competitors for leading biologicals. Amgen and other biotech pioneers are most vulnerable. E.U. patent protection for native human erythropoietin falls away in 2004. Initial U.S. patents also expire in 2004, but other patents provide protection against undifferentiated generic entry through 2012.

**Investment Conclusion**

We reiterate our outperform rating on Roche with a target price of CHF138. The progression of the phase II pipeline adds another dimension to the stock's attractiveness, which we see as a story of superior revenue growth and margin expansion. Continued new product flow and organic sales growth should position Roche for compound EPS growth of 11.0% from 2002 to 2007. CERA is the phase II product with the most potential, and increased visibility on CERA could augment interest on the stock. In addition, positive Genentech and Roche results could provide upside to our view and Roche's valuation; negative results could have an opposite effect.

We rate Amgen market-perform with a target price of $66. We believe the stock is fairly valued in that range based on both intrinsic value and relative multiple valuations. We expect competition to increase for all three of the company's key franchises and see limited immediate impact from the company's pipeline. The EPO franchise was 48% of Amgen's 2002 revenue, and we expect it to be 47% of 2008 revenue and 42% of 2003 to 2008 revenue growth. We do not anticipate that the company's late stage pipeline can contribute sufficient revenue to maintain growth at the level of industry peers.

**Details**

**Introduction: Answering the Billion-Dollar Question, "Can CERA Get to the U.S. Market?"**

We expect the U.S. erythropoietin market, currently a duopoly between Amgen and Johnson & Johnson, to achieve $6.6 bn in 2003 sales, with 9.3% compound annual growth expected to drive the market to $10.3 bn potential in 2008. In comparison, the ex-Japan/ex-U.S. segment includes Amgen and J&J but also includes Roche and Aventis. Furthermore, outside the U.S. and E.U., other biotechs, such as Dragon Pharmaceuticals, have already launched generic versions of EPO. These markets will achieve $2.7 bn in 2003 sales and should generate 10% compound growth to $4.3 bn in 2008. We expected generic versions of Epogen/Eprex to have entered the market in Europe in 2005. Such generic products are already available in developing markets, such as Brazil and non-E.U. Eastern Europe.

Roche's CERA (R744, "continuous erythropoiesis receptor activator") represents Roche's vehicle to enter the large and growing U.S. market, as well as an attempt to address the competitive threat to Roche's European market share position posed by Amgen's Aranesp. Roche's current EPO product, NeoRecormon, is sold in Europe, but not the U.S. In July 2001, Roche settled European patent disputes with Johnson & Johnson, Amgen and Genetics Institute (Wyeth) concerning recombinant EPO. Although the terms of the agreement are not public, we suspect the sale of NeoRecormon in Europe and not in the U.S. could be based on that agreement, as well as the existence of Amgen patents in the U.S. covering erythropoietin. Roche's development of CERA appears to be the culmination of a concerted effort to simultaneously design around both the agreement and Amgen's erythropoietin patents. Because Roche has previously tried unsuccessfully to enter the U.S. market, great market debate exists over Roche's present efforts.

In answering the question of whether CERA can get to the U.S. market, we anticipate that three key issues will determine CERA's potential and its relative threat: CERA's clinical profile, the viability of Roche's

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

patent challenge and the product's ability to compete against erythropoietin generics. Our conversations with opinion leaders suggest that the safety and efficacy of CERA will at least be equivalent to currently available EPO products. Though we remain uncertain about the structure of the CERA molecule, our proprietary legal analysis of available data leads us to believe that Roche should be able to counter the upcoming legal challenge from Amgen. Lastly, we believe that true generics will enter the E.U. market late in 2005. On the other hand, we expect Amgen's U.S. patent position for native human erythropoietin to remain protected through 2012. We believe CERA, by virtue of its differences from native human erythropoietin, should gain access to the market in 2007 and thus have years to establish a presence in the U.S. market prior to entry of generics.

**Overview of Erythropoietin Products and Patent Positions**

CERA is a form of human erythropoietin (EPO), an important hormone produced by the healthy kidney in very small quantities and released in response to decreased levels of oxygen in body tissue. Therapeutically, EPO products are used to raise or sustain red blood cell levels and to decrease the need for transfusions in patients with anemia. Currently approved EPO products in U.S. and European markets include: Epogen (Amgen), Aranesp (Amgen), Procrit (Johnson & Johnson), Eprex (Johnson & Johnson), Dynepo (Transkaryotic/Aventis), and NeoRecormon/Epogin[1] (Roche/Chugai). (**Exhibit 1**) Differences in glycosylation[2] differentiate these products: Epogen, Eprex and Procrit are generically known as epoetin alfa, Aranesp as darbepoetin alfa, Dynepo as epoetin delta, and NeoRecormon as epoetin beta.



[1] Roche distributes NeoRecormon as "Epogin" in Japan through Chugai.

[2] Certain proteins produced recombinantly by eukaryotic cells are modified with one or more oligosaccharide groups. This modification is known as glycosylation. Glycosylation occurs at specific locations on the protein molecule and includes two types of oligosaccharide groups: O-linked and N-linked. Human erythropoietin has an amino acid sequence of 165 amino acid residues and includes three N-linked oligosaccharides and one O-linked oligosaccharide.

**Catherine J. Arnold** • arnoldcj@bernstein.com • +1-212-756-1885

Exhibit 1
**Comparison of CERA to Erythropoietins Approved in U.S. and European Markets**

| Brand | Epogen | Aranesp | Procrit | Eprex | NeoRecormon | Dynepo | CERA |
|---|---|---|---|---|---|---|---|
| Product | epoetin alfa | darbepoietin alfa | epoetin alfa | epoetin alfa | epoetin beta | epoetin delta | Unknown |
| Marketer | Amgen | Amgen | J&J | J&J | Roche | TKT/Aventis | Roche |
| Territory | US | WW | US | OUS | OUS | OUS | WW |
| Manufacturer | Amgen | Amgen | Amgen | J&J | Roche/BMC | Lonza Biologics | Roche |
| Production | CHO Cells | CHO Cells | CHO Cells | CHO Cells | CHO Cells | Human cells | ? |
| Differences to native | None | 2 amino acids | None | None | None | None | ? amino acids |
| | None | Novel glycosylation | None | None | None | None | Novel glycosylation |
| Molecular Wt | 30,400 kDa | 37,000 kDa | 30,400 kDa | 30,400 kDa | 30,400 kDa | ?30,400 kDa | ? |
| Administration | IV or SC | IV or SC | IV or SC | IV only | SC or IV | SC or IV | IV or SC |
| Dosing | 3 doses/wk | Q 1-2 weeks | 3 doses/wk | 3 doses/wk | ≤ Q 1 week | 2-3 doses/wk | □Q 4 weeks |
| Units | 2,3,4,10,000 units/ml | 25,40,60 µg/ml | 2,3,4,10,000 units/ml | 2,3,4,10,000 units/ml | 0.5,1,2,3,4,5,6,10,000 units/0.3ml | 2,3,4,10,000 units/ml | ? |
| Dose Form | 1 ml vials | 1 ml vials | 1 ml vials | 1 ml vials | 0.3 ml prefilled syringes/1ml vials | 1 ml vials/0.5ml syringes | ? |
| US Approval | Jun-89 | Sep-01 | Jun-89 | not marketed | not marketed | not approved | 2006E |
| EU Approval | not marketed | Jun-01 | not marketed | 1991 | Jul-97 | Mar-02 | 2006E |
| AWP | $140.20/1ml vial | $199.50/40µg 1ml vial | $147.44/1ml vial | na | na | na | ? |
| Dose | 50-150iu/kg/tiw | 6.25-200ug/q1-2wks | 50-150iu/kg/tiw | na | na | 50 - 150 iu/kg/biw-tiw | ? |
| Cost/patient/year | $21,871 | $15,561 | $23,001 | na | na | na | ? |
| Cost Basis | 1x10,000 iu tiw | 1x60µg qw | 1x10,000 iu tiw | na | na | na | ? |
| Stabilizer | HSA | HSA/polysorbate | HSA | HSA-->Polysorbate | Polysorbate | Polysorbate | ? |
| Presentation | Liquid | Liquid | Liquid | Liquid | Liquid | Liquid | Liquid |
| Storage | Refrigerated | Refrigerated | Refrigerated | Refrigerated | Refrigerated | Refrigerated | Non-refrigerated |
| Shelf Life | 24 months | 24 months | 24 months | 24 months | 36 months | 24 months | ? |
| Patent Situation | Amgen holds key patents | Amgen holds key patents | Amgen licensed to J&J | Amgen licensed to J&J | Roche, J&J & Amgen settled longstanding litigation in 2001 | Ongoing litigation between TKT and Amgen | Impending litigation with Amgen |

Source: EMEA, Product Package Inserts, Bernstein Analysis

### CERA Appears to be an Erythropoietin with Altered Glycosylation Sites; We Suspect it Has Altered Amino Acid Sequences

We understand from Roche's public disclosure in Berlin in June 2003 that CERA consists of a single methoxy-polyethylene glycol ("PEG") molecule bound to a modified synthetic erythropoietin protein backbone. In view of the two Roche patents relating to erythropoietin derivatives (discussed later), we suspect that the underlying erythropoietin molecule in CERA is a derivative of human erythropoietin that includes certain amino acid sequence substitutions, deletions or additions that result in a change to one or more glycosylation sites on the erythropoietin molecule. However, at present, we do not know the exact nature of the substitutions, but assume at least one amino acid difference will be required to establish uniqueness and evade Amgen's patents.

Our view of an altered amino acid sequence for CERA is supported by discussions with industry sources that suggest that CERA is the culmination of an erythropoietin amino acid sequence reengineering process that began in 1991 after Genetics Institute – from which Boehringer Mannheim (since acquired by Roche) and Chugai licensed NeoRecormon and Epogin, respectively – lost its litigation with Amgen in the U.S. Genetics Institute had obtained a U.S. patent on the natural form of erythropoietin in 1987; however, Amgen obtained a patent on the process and cell lines used in producing human erythropoietin, as well as for the amino acid sequence of erythropoietin. By 1991, the Washington D.C. Court of Appeals had overturned essential claims in Genetics Institute's patent, closing the opportunity for Genetics Institute and licensees to enter the U.S. market. Despite that setback, Genetics Institute and partners have since had considerable time to reengineer human erythropoietin.

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

**Available Clinical Data Shows CERA to be Safe, Effective and Differentiated**

CERA appears to have completed a series of well-designed randomized phase II clinical trials in the U.S. (and is in phase I trials in Japan) in anemic patients with renal disease and cancer. Discussions with clinical leaders suggest that the phase II trials in the U.S. are well-controlled and incorporate hundreds of patients. To date, Roche has released relatively little data on CERA. **Exhibit 2** provides a summary of the information we know to date about CERA. We suspect that the dearth of information is linked to competitive considerations in advance of the impending litigation with Amgen.[3] Opinion leaders working on CERA clinical trials have expressed little concern over publicly available information based on what they know of CERA. The next major dataset on CERA will come at the American Society of Nephrology's "Renal Week 2003," from November 12th to 17th in San Diego, California.

Exhibit 2
**Summary of Currently Available Information on CERA**

**Status in clinical trials**
- Completed or soon to complete well-controlled phase II trials in oncology and renal indications
- Phase III trials expected to start in 1Q 2004

**Pharmacokinetics/pharmacodynamics**
- Potential to ensure stronger and longer persisting correction of the hemoglobin values than at present available
- Capability of molecule to quickly detach from EPO receptor and to re-bind is responsible for unique activity
- Potential for monthly to every-six-weeks dosing
- Serum half-life of 80 to 120 hours by IV and up to 150 hours when given as a subcutaneous injection
- Currently available products with maximum serum half-life of 25 hours by IV and 48 hours by subcutaneous
- Subcutaneous and IV application provide comparable results

**Safety**
- Low potential for immunogenicity

Source: Bernstein analysis

*Data from World Congress in Berlin differentiated CERA from NeoRecormon*

In June 2003, Roche presented CERA data at the World Congress of Nephrology meeting in Berlin, German. We understand that, at that meeting, Roche disclosed that the CERA contains a single PEG molecule that is bound to a modified synthetic erythropoietin molecule. This polymer appears to extend the half-life of the compound relative to NeoRecormon. The presentation did not elucidate the extent of CERA's homology to epoetin beta. However, the data presented show that CERA binds less tightly to the erythropoietin receptor than epoetin beta, and was able to induce greater stimulation of erythropoiesis than epoetin beta (both in terms of magnitude and duration), suggesting that the protein molecule underlying CERA differs chemically from epoetin beta. Furthermore, data in Berlin showed CERA's half-life in animals to be two- to seven-times greater than epoetin beta. We understand CERA to be potentially suitable for once-monthly administration, rather than once every other week for Amgen's Aranesp and once weekly for NeoRecormon, and to potentially be suitable for room temperature storage, unlike other erythropoietin products that must be kept refrigerated. This product is likely to be very attractive to patients and physicians in the most rapidly growing segment of the erythropoietin market, oncology. By 2008, we

[3] In Aranesp's development, Amgen took a similarly coy strategy leading into legal proceedings with Johnson & Johnson. After the initiation of proceedings, Amgen was more forthcoming with Aranesp data. We expect a similar pattern with Roche and CERA.

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

forecast that oncology sales of EPO products will be 34% of the U.S. market ($2 bn). Once per treatment cycle dosing is more convenient and cost effective for oncology patients, physicians and payors.

*CERA has low potential for immunogenicity*

All therapeutic proteins, including CERA, potentially may induce immune responses. Fears about increased immunogenicity for CERA were fed by post-marketing surveillance data which showed an increase rate of pure red cell aplasia[4] (PRCA) in patients taking Eprex subcutaneously for chronic renal failure. E.U. health authorities have since imposed restrictions on the use of Eprex subcutaneously. This effect, which we believe is real and largely, but not exclusively, limited to Eprex, most likely resulted from the changes to J&J's production process and stabilizer formulation at its Puerto Rico production facility. The effect has not been attributed, at least at any increased rate, to other recombinant erythropoietin products.

For the following reasons, we do not see immunogenicity as a significant risk for CERA:

- To date, CERA has not shown immunogenicity (i.e. anti-erythropoietin antibodies) in normal human volunteers, cancer patients or dialysis patients. Though the incidence of antibody development in patients receiving CERA has not been adequately studied, CERA likely has had enough patient-years—perhaps 3,000 to 4,000 patient-years—of experience for PRCA cases to emerge.
- Second, the increased incidence of PRCA seen with Eprex has not been attributed, at least at any increased rate, to other recombinant erythropoietin products, despite Eprex's similarity to these products. In addition, the problem with Eprex emerged after a change in manufacturing; that is, immunogenicity had not been a problem with Eprex all along. Thus, current thinking is that the increased risk of PRCA is likely tied directly to the manufacturing of Eprex itself.
- Third, CERA is a pegylated protein[5], and pegylation in general is not associated with increases in immunogenicity. To the contrary, pegylation is associated with decreased immunogenicity. The only case of increased immunogenicity with pegylation of which we are aware is with thrombopoietin, and immunogenicity likely resulted because the pegylated product was not only pegylated, but also truncated.

*We suspect CERA's pharmacokinetics, at the very least, allow for improved dosing*

Much of the excitement that the market has about CERA comes from the perception that CERA is a more potent, and therefore more effective, erythropoietin. Whether or not CERA is more potent remains to be proven. The feeling among opinion leaders, however, is that CERA's pharmacokinetics at the very least may result in improved dosing. For current erythropoietins, if one corrects for dosing, the products are essentially equal in ability to improve patient outcomes. Longer-acting erythropoietins, like CERA and Aranesp, have convenience advantages for patients and physicians over shorter-acting ones in non-dialysis patient groups.



[4] Pure red cell aplasia is characterized by a near absence of red blood cell precursors in the bone marrow. The result is sub-clinical to severe anemia.

[5] Pegylation is a process whereby polyethylene glycol (PEG) is attached to a protein in order to prolong protein activity by permitting substances to stay in the body for a longer time before they are metabolized and eliminated.

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

*Q4-week dosing for CERA and possibly Aranesp may help expand the category*

Due to the lack of an FDA approved indication, cancer patients not on chemotherapy, and patients with anemia of chronic disease (e.g. rheumatoid arthritis, Crohn's disease), are currently unable to have erythropoietin (EPO) treatment reimbursed. The initial studies of EPO in these indications failed to achieve statistical significance. The FDA therefore has not approved EPO for these indications and as a result, in most states in the U.S., CERA's use is minimal. Oddly enough, anecdotal evidence exists from physicians that EPO products work better in cancer patients that are not on chemotherapy and for patients with anemia of chronic disease. An optimal dosing schedule for EPO in these settings might show benefit in the future. CERA's dosing schedule may or may not provide advantage over past attempts to show efficacy in this setting. The potential for a once-monthly protocol for CERA may also be more desirable to these patient populations. It has also been suggested that CERA could go to a once-every-six weeks dosing schedule but we don't expect this will add to the promise in this setting. Our thinking is that the need to monitor a patients red blood cell count at a frequency of not less than once-monthly, may limit the benefit of an every 6-week regimen. Aranesp may also be dosed every four weeks, and we expect CERA to compete head-to-head. The data on every four-week dosing for Aranesp is still preliminary, but we expect Amgen to actively pursue the claim and dosing based on the early data to compete effectively with CERA.

**CERA's Two U.S. Patents Shed Some Light on Its Structure and Clinical Properties**

Insight on CERA has also come from a review of CERA's patent portfolio by our outside legal counsel. Counsel conducted a search for patents owned by Roche as well as Chugai Pharmaceuticals and found two patents issued in 2002 and 2003 covering PEG-erythropoietin conjugates in which the erythropoietin molecule differs from human erythropoietin by the addition or rearrangement of one or more glycosylation sites. The patents include U.S. Patent No. 6,340,742 (issued January 22, 2002) and U.S. Patent No. 6,583,272 (issued June 24, 2003). Both patents describe increased half-life for these conjugates and increased production of reticulocytes in comparison to human erythropoietin. (**Exhibit 3**) This information is consistent with the data presented at June 2003 conference in Berlin. To the extent CERA includes a derivative of human erythropoietin, and CERA is covered by one or both of the patents, then Roche will have patent protection for CERA until June 2020, ignoring any FDA awarded extensions and assuming the patents withhold any validity challenges.

Exhibit 3
**Summary of CERA Patents**

| Patent Number | Issued | Expected Expiry | Key Claims |
|---|---|---|---|
| 6,340,742 | 22-Jan-02 | 17-Nov-19 | • Conjugate comprising an erythropoietin glycoprotein |
| 6,583,272 | 24-Jun-03 | 30-Aug-19 | • Conjugate comprising an erythropoietin glycoprotein |

Source: Proprietary legal analysis, Bernstein analysis

**CERA Patents will be Subject to Scrutiny against Amgen's Patents for both Epogen and Aranesp**

Amgen's patents and their coverage are summarized in **Exhibit 4** and discussed thereafter:

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

Exhibit 4
**Summary of Amgen's Erythropoietin Patents and Our View Vis-à-vis CERA**

| Patent Number | Expected Expiry | Key Claims | Our View |
|---|---|---|---|
| **Epogen** | | | |
| 4,703,008 | 27-Oct-04 | • Specific amino acid sequences encoding EPO | Not relevant |
| 5,955,422 | 27-Oct-04 | • Pharmaceutical composition comprising a therapeutically effective amount of human erythropoietin | Lack of enablement relating to derivative |
| 5,441,868 | 15-Aug-12 | • Processes for production of EPO | Lack of enablement relating to derivative |
| 5,618,698 | 15-Aug-12 | • Processes for production of EPO | Not relevant |
| 5,621,080 | 20-Aug-13 | • Specific amino acid sequences encoding EPO | Not relevant |
| 5,547,933 | 20-Aug-13 | • Non-naturally occuring EPO glycoprotein products<br>• Found invalid as indefinite vs. Transkaryotic | Can not be asserted |
| 5,756,349 | 26-May-15 | • Vertebrate cell propagation to produce EPO<br>• Other process for producing EPO | Lack of enablement relating to derivative |
| **Aranesp** | | | |
| Pending | Pending | • Pending | Too narrow |

Source: Proprietary legal analysis, Bernstein analysis

*Amgen's Epogen Patents Expiring in October 2004*

**U.S. Patent No. 4,703,008 ("the '008 patent")** expires on October 27, 2004. The '008 patent was previously litigated in 1991, and as a result of the litigation, the broad claims were invalidated. The remaining claims are limited to specific DNA sequences encoding native human erythropoietin. Therefore, *we do not believe this patent will be relevant to the CERA product.*

**U.S. Patent No. 5,955,422 ("the '422 patent")** is also believed to expire on October 27, 2004. The broadest claim of the '422 patent covers a pharmaceutical composition comprising a therapeutically effective amount of human erythropoietin. This patent was asserted against Transkaryotic Therapies, and the lower court upheld the validity of the broadest claim. The validity of the claim was appealed, and the Appeals court vacated the prior decision and remanded the case back to the district court. We suspect that Amgen would argue that the term "human erythropoietin" covers derivatives of human erythropoietin. Roche would argue this term is limited to native human erythropoietin and does not cover derivatives, and if a court would construe the term to cover derivatives, then the claim would be invalid for lack of enablement. Lack of enablement in this context essentially means that the '422 patent, if interpreted to cover all erythropoietin derivatives, would be invalid since the patent does not teach how to make all erythropoietin derivatives. Under U.S. patent law, the scope of the claim coverage must be matching in scope with the teachings of the specification. The '422 patent simply does not teach how to make the potentially thousands of derivatives that may be encompassed by "erythropoietin derivatives." In view of the enablement issue, a court would likely determine that "human erythropoietin" is limited to the human form and does not cover derivatives. *Under current U.S. case law, we suspect that Roche would have the stronger position if this patent were asserted against CERA.*

*Amgen's Epogen Patents Expiring in 2012-2015*

**U.S. Patent No. 5,441,868** ("the '868 patent") expires on August 15, 2012. The broadest claims of the '868 patent are directed to processes for producing glycosylated erythropoietin polypeptides having the *in vivo* property of causing bone marrow cells to increase production of reticulocytes and red blood cells by the following two steps: (a) growing mammalian host cells transformed or transfected with an isolated DNA

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

sequence encoding human erythropoietin; and (b) isolating said glycosylated erythropoietin polypeptide therefrom. Here again, we suspect that Amgen would argue that the term "human erythropoietin" covers derivatives of human erythropoietin. Roche would argue this term is limited to native human erythropoietin and does not cover derivatives, and if a court would construe the term to cover derivatives, then the claim would be invalid for lack of enablement. *Under current U.S. case law, we suspect that Roche would have the stronger position if this patent were asserted against CERA.*

**U.S. Patent No. 5,618,698** ("the '698 patent") also expires on August 15, 2012 and claims processes for the production of erythropoietin. However, the claims of this patent are limited to specific DNA sequences. Assuming Roche's CERA amino acid sequence differs from the native protein, *we do not believe this patent will be relevant to the CERA product.*

**U.S. Patent No. 5,621,080** (the "080 patent") expires on August 20, 2013. The patent contains claims for isolated erythropoietin glycoprotein, an isolated polypeptide, and a therapeutically effective pharmaceutical composition. This patent was asserted against Transkaryotic Therapies, and the lower court upheld the validity of the claims. The decision was heard on appeal, and the lower court decision was vacated and the case was remanded back to the district court. Notwithstanding the remand, the claims of the '080 patent are limited to a specific amino acid sequence. Therefore, *we do not believe this patent will be relevant to the CERA product.*

**U.S. Patent No. 5,756,349** ("the '349 patent") expires on May 26, 2015. This patent includes claims directed to vertebrate cells propagated to produce erythropoietin and a process for producing erythropoietin. The claims also require that transcription is controlled by non-human transcription control DNA sequences, and that a certain amount of erythropoietin is produced. This patent was asserted against Transkaryotic Therapies, and the lower court upheld patent validity. The decision was appealed to the Appeals court, and the Appeals court vacated the prior decision and remanded the case back to the district court. Here again, assuming other elements of the claims are met in the process that Roche would use to make the CERA product, Amgen would argue that the term "erythropoietin" covers derivatives of human erythropoietin. Roche would presumably argue this term is limited to native human erythropoietin and does not cover derivatives, and if a court would construe the term to cover derivatives, then the claim would be invalid for lack of enablement. Again, *under current U.S. case law, we suspect that Roche would have the stronger position if this patent were asserted against CERA.*

**U.S. Patent No. 5,547,933** ("the '933 patent") expires on August 20, 2013. The broadest claims are directed to non-naturally occurring erythropoietin glycoprotein products. This patent was asserted against Transkaryotic Therapies, and the lower court found all claims to be invalid as indefinite. The appeals court affirmed the decision. Therefore, *this patent cannot be asserted against CERA.*

*Amgen's Aranesp Patents Pose Surmountable Hurdles for CERA Entry to U.S. and European Markets*

An additional obstacle for Roche's CERA patents may come from newer Aranesp patents that are pending in the United States. Aranesp contains two additional N-linked carbohydrate chains conjoined to human erythropoietin. From the research of our outside legal counsel, we suspect that Aranesp differs from human erythropoietin in the amino acid substitutions to native human erythropoietin: Asn30 Thr 32 Val 87 Asn 88 Thr 90. We understand that Amgen filed a Patent Cooperation Treaty[6] (PCT) application in August 1994 that includes one or more claims that cover the molecule in Aranesp. The PCT application was published in February 1995 under PCT publication number WO 95/05465A1. The PCT application claims priority to U.S. application No. 08/108,016 filed on August 17, 1993. Our search for U.S patents and published

[6] The Patent Cooperation Treaty enables an applicant to seek patent protection for an invention simultaneously in each of a large number of countries by filing an "international" patent application.

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

applications did not uncover any patent or application relating to U.S. application No. 08/108,016. Therefore, we suspect that Amgen is still prosecuting that application (or a continuation application of that application) at the U.S. Patent Office.

The PCT application was filed in Europe and other countries. The corresponding European application was allowed and issued as European Patent No. EP 0 640 619 B1, and the grant of the patent was published on July 23, 1997. In 1998, Boehringer Mannheim (now part of Roche) filed an opposition to the Aranesp European patent, and Roche continued the opposition after acquiring Boehringer Mannheim. The Opposition Division of the European Patent Office issued a decision on the opposition on August 1, 2001; yet, the claims of the European patent were maintained with a few amendments. Roche appealed the decision of the Opposition Division in September 2001, and the appeal is still pending. Given Roche's initial opposition to the Aranesp patent and subsequent appeal, there is some market concern that Aranesp claims cover CERA. Additional uncertainty exists in the U.S. market since the Aranesp U.S. patent application, which corresponds to the patent involved in the European appeal, has not yet issued as a patent.

Although, the uncertainty of the Aranesp patent in the U.S. may be a risk to our hypothesis that Roche will be able to circumvent Amgen's intellectual property and enter the U.S. market, what we know to date supports our view more than not. Details are as follows.

The Aranesp European patent is based upon a U.S. application that was filed in August 1993, which was subsequently published as a European PCT application in February 1995.

- In view of this February 1995 publication of the Aranesp U.S. patent application, we suspect that Roche was aware of the claims of the Aranesp patent application and either took steps to design CERA around these claims, considered the claims not to cover the CERA product, or believed that the claims were invalid.
- Further, although Roche opposed the European patent, this opposition is not an indication that the European patent covers CERA. Rather, it is customary for competitors to oppose one another's European patents to add cushion to competitive dynamics.
- In addition, Amgen does not have equivalent patent protection in the U.S. despite the filing of a U.S. application over 10 years ago (August 1993). We can only speculate as to why this patent has not been granted. The reasons may run the gamut including: the U.S. Patent and Trademark Office (USPTO) would not grant the claims sought by Amgen because the USPTO did not consider the claims to be patentable, and, Amgen is currently still fighting with the USPTO or decided to abandon the case. Alternatively, the application or its continuation is involved in an interference proceeding with another party (ies) at the U.S. Patent and Trademark Office to determine the priority of invention.

**Impending Litigation May Begin Once CERA Comes Close to Filing or Launch**

Though Amgen has yet to initiate legal proceedings against Roche, litigation could start at any time. Amgen may want to wait to initiate legal proceedings until close to the filing and launch of CERA so that the ongoing status of litigation forces Roche to decide whether to launch CERA at risk. We suspect that Roche is optimistic enough about CERA's patent position to launch at risk.

**Worldwide Generic Entry: Europe in 2005, but Not Until 2012 in the U.S.**

True generic entry will not occur in biopharmaceutical markets. Individual product, process and plant approvals are inseparable from clinical data supporting each product's approval. Nevertheless, the economic stakes are high, and competitors are actively developing direct and modified competitors for leading biologicals, including erythropoietin products. Amgen and other biotech pioneers are most

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

vulnerable. E.U. patent protection for native human erythropoietin falls away in 2004, and we expect true generics will enter the E.U. market late in 2005 after Amgen's patents lapse. Because much of erythropoietin use in Europe is for renal disease and governments pay for a majority of erythropoietin, we forecast significant generic uptake. In the U.S., certain patents also expire in 2004, but other patents provide protection against undifferentiated generic entry through 2012. We believe generic uptake will be lower in the U.S. because physicians will not substitute generic native human erythropoietin for the differentiated, longer acting products, Aranesp and CERA, which will be used preferentially in oncology applications to match treatment cycles.

### CERA Forecast and Impact on Amgen

Post our proprietary legal analysis, conversations with opinion leaders, and further due diligence on CERA, we believe Roche has a stronger patent position than Amgen if Amgen's native human erythropoietin patents are asserted against CERA. **Exhibit 5** shows our new erythropoietin market forecasts in the U.S. and Europe.

Exhibit 5
**Erythropoietin U.S. and ex-U.S./ex.-Japan Market Forecasts (in $ mm)**

| | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | '03 to '08 CAGR |
|---|---|---|---|---|---|---|---|---|
| **Total** | **$7,815** | **$9,286** | **$10,686** | **$11,905** | **$12,920** | **$13,826** | **$14,636** | *9.5%* |
| *YoY Growth* | *29.1%* | *18.8%* | *15.1%* | *11.4%* | *8.5%* | *7.0%* | *5.9%* | |
| **U.S.** | **$5,579** | **$6,621** | **$7,572** | **$8,417** | **$9,153** | **$9,787** | **$10,333** | *9.3%* |
| *YoY Growth* | *24.4%* | *18.7%* | *14.4%* | *11.2%* | *8.7%* | *6.9%* | *5.6%* | |
| Procrit | 3,034 | 3,046 | 3,408 | 3,746 | 3,982 | 4,111 | 3,823 | *4.7%* |
| *YoY Growth* | *29.9%* | *0.4%* | *11.9%* | *9.9%* | *6.3%* | *3.2%* | *(7.0%)* | |
| Epogen | 2,261 | 2,582 | 2,764 | 2,988 | 3,112 | 3,132 | 3,203 | *4.4%* |
| *YoY Growth* | *7.2%* | *14.2%* | *7.0%* | *8.1%* | *4.1%* | *0.6%* | *2.3%* | |
| Aranesp | 285 | 993 | 1,401 | 1,683 | 2,059 | 2,349 | 2,583 | *21.1%* |
| *YoY Growth* | *NM* | *248.8%* | *41.1%* | *20.2%* | *22.3%* | *14.1%* | *10.0%* | |
| CERA | - | - | - | - | - | 196 | 723 | *NM* |
| *YoY Growth* | *NM* | *NM* | *NM* | *NM* | *NM* | *NM* | *269.5%* | |
| Other | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| *YoY Growth* | *NM* | *NM* | *NM* | *NM* | *NM* | *NM* | *NM* | |
| **Ex-U.S., Ex-Japan** | **$2,236** | **$2,666** | **$3,114** | **$3,488** | **$3,767** | **$4,038** | **$4,303** | *10.1%* |
| *YoY Growth* | *42.6%* | *19.2%* | *16.8%* | *12.0%* | *8.0%* | *7.2%* | *6.5%* | |
| Eprex | 1,235 | 1,199 | 1,214 | 1,186 | 1,168 | 1,010 | 947 | *-4.6%* |
| *YoY Growth* | *12.9%* | *(2.9%)* | *1.2%* | *(2.4%)* | *(1.5%)* | *(13.5%)* | *(6.2%)* | |
| NeoRecormon | 870 | 933 | 1,090 | 1,116 | 1,130 | 1,090 | 990 | *1.2%* |
| *YoY Growth* | *85.5%* | *7.2%* | *16.8%* | *2.4%* | *1.3%* | *(3.5%)* | *(9.2%)* | |
| Aranesp | 131 | 533 | 810 | 1,011 | 1,017 | 1,030 | 1,011 | *13.7%* |
| *YoY Growth* | *NM* | *307.3%* | *51.9%* | *24.9%* | *0.6%* | *1.3%* | *(1.8%)* | |
| CERA | - | - | - | - | - | 61 | 194 | *NM* |
| *YoY Growth* | *NM* | *NM* | *NM* | *NM* | *NM* | *NM* | *219.6%* | |
| Other | - | - | - | 174 | 452 | 848 | 1,162 | *NM* |
| *YoY Growth* | *NM* | *NM* | *NM* | *NM* | *159.2%* | *87.6%* | *37.0%* | |

Source: Company Reports, Bernstein analysis

*Changes to Roche Forecasts*

Because we feel that CERA's patents are sound and that the compound's pharmacokinetics confer positive patient outcomes, we have increased Roche's CERA worldwide forecasts from $79 mm (CHF105 mm) to $256 mm (CHF341 mm) in 2007 and from $143 (CHF190 mm) to $917 mm (CHF1,222 mm) in 2008. Some of CERA gains cannibalize NeoRecormon sales in Europe, so we have decreased our NeoRecormon

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

worldwide forecasts from CHF1,974 mm to CHF1,802 mm in 2008. These changes result in a CHF0.06 increase in 2007 EPS and a CHF0.21 increase in 2008 EPS (**Exhibit 6**). Our 2003E to 2008E EPS growth rate goes from 15.2% to 15.7%. CERA now accounts for 2.7% of Roche Group 2008 sales and 7.3% of 2003 to 2008 sales growth.

Exhibit 6
**Roche Group: Worldwide Erythropoietin Franchise Forecast Revisions (in CHF mm) and Impact on EPS (in CHF)**

| | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 03 to '08 CAGR |
|---|---|---|---|---|---|---|---|---|
| **CERA** | | | | | | | | |
| Sales, Old | - | - | - | - | - | CHF 105 | CHF 190 | *NM* |
| Sales, New | - | - | - | - | - | 341 | 1,222 | *NM* |
| Difference | - | - | - | - | - | CHF 236 | CHF 1,032 | |
| **NeoRecormon** | | | | | | | | |
| Sales, Old | CHF 1,192 | CHF 2,131 | CHF 2,451 | CHF 2,483 | CHF 2,359 | CHF 2,194 | CHF 1,974 | *-1.5%* |
| Sales, New | 1,192 | 2,131 | 2,451 | 2,483 | 2,359 | 2,194 | 1,802 | *-3.3%* |
| Difference | - | - | - | - | - | - | (CHF172) | |
| **Roche Group** | | | | | | | | |
| Sales, Old | CHF 26,546 | CHF 29,183 | CHF 32,894 | CHF 36,926 | CHF 39,760 | CHF 42,581 | CHF 44,980 | *9.0%* |
| Sales, New | 26,546 | 29,183 | 32,894 | 36,926 | 39,760 | 42,818 | 45,840 | *9.5%* |
| Difference | - | - | - | - | - | CHF 236 | CHF 860 | |
| **Roche EPS** | | | | | | | | |
| EPS, Old | CHF 5.09 | CHF 4.52 | CHF 5.84 | CHF 6.38 | CHF 7.78 | CHF 8.59 | CHF 9.17 | *15.2%* |
| EPS, New | 5.09 | 4.52 | 5.84 | 6.38 | 7.78 | 8.65 | 9.38 | *15.7%* |
| Difference | - | - | - | - | - | CHF 0.06 | CHF 0.21 | |

Source: Company Reports, Bernstein analysis

*Changes to Amgen Forecasts*

We expect the launch of CERA to slow the growth of Amgen's erythropoietin franchise, particularly the sales of Aranesp in the U.S. market due to both products' expected use in the oncology market. We forecast total Amgen worldwide erythropoietin franchise sales of $6.9 bn in 2008, consisting of $3.2 bn of Epogen and $3.7 bn of Aranesp, implying compound annual growth rates from 2003 of 12%, 5% and 19% for the franchise, Epogen and Aranesp, respectively. Prior to taking into account CERA, we had expected growth of 6% and 20%, for the individual products and overall franchise growth of 13%. For Aranesp, we expect U.S. and E.U. sales of $2.6 bn and $1.0 bn, which are approximately $200mm and $100mm lower than our forecasts prior to the incorporation of CERA in our forecast. (**Exhibit 7**) The major effects of patent expiry on Amgen are the result of generic entry slowing market growth in Europe. In the U.S., we have previously anticipated new competitors in 2007 to 2010. As a result of our analysis of CERA, and Roche's patent position, we have increased our share loss assumptions above our previous forecast.

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

Exhibit 7
**Amgen: Worldwide Erythropoietin Franchise Forecast Revisions (in $ mm)**

**Amgen Forecast- Including CERA**

| | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 03-08 CAGR |
|---|---|---|---|---|---|---|---|---|
| Epogen | $2,261 | $2,440 | $2,633 | $2,813 | $2,986 | $3,157 | $3,185 | 5% |
| *% growth* | | *8%* | *8%* | *7%* | *6%* | *6%* | *1%* | |
| Aranesp | | | | | | | | |
| US | $285 | $993 | $1,428 | $1,648 | $2,005 | $2,370 | $2,635 | 22% |
| EU | 131 | 533 | 825 | 990 | 990 | 1,039 | 1,031 | 14% |
| Total | $416 | $1,526 | $2,253 | $2,639 | $2,996 | $3,409 | $3,666 | 19% |
| *% growth* | | *NM* | *48%* | *17%* | *14%* | *14%* | *8%* | |
| EPO Franchise | $2,677 | $3,966 | $4,887 | $5,452 | $5,982 | $6,565 | $6,852 | 12% |
| *% growth* | | *48%* | *23%* | *12%* | *10%* | *10%* | *4%* | |

**Amgen Forecast- Excluding CERA**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Epogen | $2,261 | $2,440 | $2,633 | $2,813 | $2,986 | $3,230 | $3,307 | 6% |
| *% growth* | | *8%* | *8%* | *7%* | *6%* | *8%* | *2%* | |
| Aranesp | | | | | | | | |
| US | $285 | $993 | $1,428 | $1,648 | $2,005 | $2,447 | $2,790 | 23% |
| EU | 131 | 533 | 825 | 990 | 990 | 1,090 | 1,076 | 15% |
| Total | $416 | $1,526 | $2,253 | $2,639 | $2,996 | $3,537 | $3,866 | 20% |
| *% growth* | | *NM* | *48%* | *17%* | *14%* | *18%* | *9%* | |
| EPO Franchise | $2,677 | $3,966 | $4,887 | $5,452 | $5,982 | $6,767 | $7,172 | 13% |
| *% growth* | | *48%* | *23%* | *12%* | *10%* | *13%* | *6%* | |

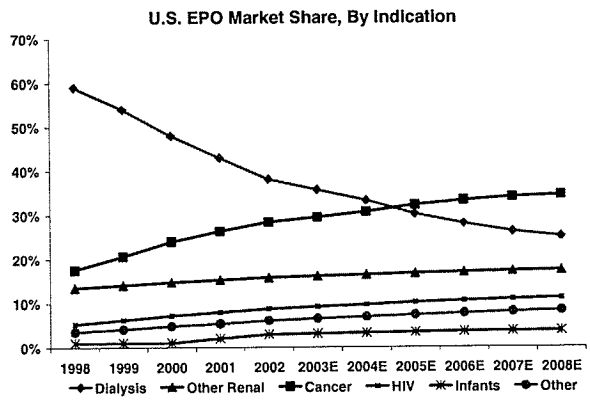
Source: Company Reports, Bernstein analysis

**Assumptions and Considerations**

We assume the EPO market decelerates from 29% year-over-year growth in 2002 to 5.9% growth in 2008 and that revenues from dialysis patients decrease from a 38% share in 2002 to a 25% share in 2008, while revenues from cancer patients increase from a 28% to a 34% contribution over the same period (**Exhibit 8**). We expect that CERA launches globally in 2007 and thereafter achieves 2% and 7% market shares in the U.S. in 2007 and 2008, respectively; and 1.5% and 4.5% market shares ex-U.S. in 2007 and 2008, respectively. We believe these share estimates are reasonable given Aranesp's 20+% market share after less than two years on the U.S. market (**Exhibit 9**). As Amgen has used Aranesp to enter the European market, Roche hopes to use CERA to enter the U.S. market. We do not expect CERA's uptake in the U.S. to approach that of Aranesp in Europe since Aranesp's uptake was bolstered by market concerns over Eprex's potential for immunogenicity, and CERA will enter a European market already being eroded by lower priced generic versions of Epogen/Eprex.

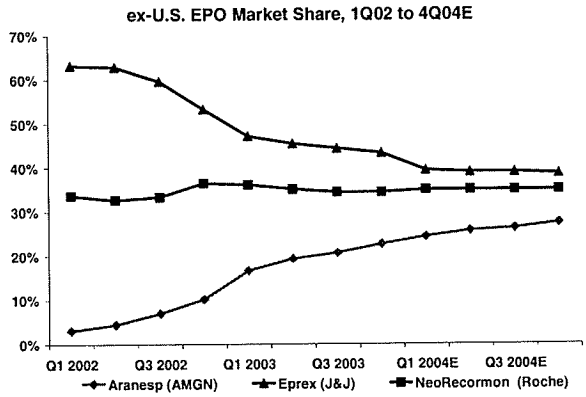
**Catherine J. Arnold** • arnoldcj@bernstein.com • +1-212-756-1885

Exhibit 8
**Relative Importance of Dialysis to Diminish**




Source: Company Reports, Bernstein analysis

Exhibit 9
**Aranesp Achieved Roughly 20% Share by Q2 2003**




Source: Company Reports, Bernstein analysis

*Other assumptions and considerations:*

- **CERA product timeline. Exhibit 10** sets forth our expectation for the developmental, regulatory and legal timeline for CERA.

Exhibit 10
**CERA Product Timeline**

| European Milestones | Timing | U.S. Milestones | Timing |
|---|---|---|---|
| Phase II complete | 2H 2003 | Phase II complete | 2H 2003 |
| Phase III begins | 1H 2004 | Leverage E.U. phase III data for U.S. registration | |
| Phase III ends | 4Q 2004 | | |
| 12 month safety data | 1Q 2005 | | |
| BLA filing | 3Q 2005 | BLA filing | 3Q 2005 |
| EMEA approval | 3Q 2006 | U.S. approval | 3Q 2006 |
| | | Amgen litigation begins | 3Q 2006 |
| Launch | 1Q 2007 | Launch at risk | 2Q 2007 |

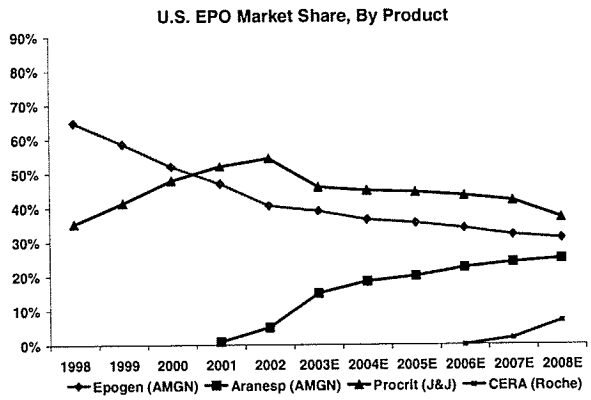
Source: Bernstein analysis

- **Competition in U.S.: Reduced pricing not just for cancer patients.** We expect that when CERA enters the U.S. market, it will gain share by launching at a modest discount to Aranesp. This is consistent with the net effect of Roche's recent launch of Pegasys and could assure immediate adoption in certain segments (e.g., Medicare). We expect the price difference to be 7.5-15%. **Exhibit 11** outlines our forecast for market share in the U.S. market.
- **Competition in Europe: Aranesp, price sensitivity as challenges.** Despite CERA's dosing characteristics, Aranesp will be able to compete in Europe in the cancer/chemo marketplace because Amgen can achieve every-three-week dosing. Amgen need not go further since cancer patients are getting chemo every three weeks. Thus, in our model CERA erodes share mostly from NeoRecormon, then Eprex, then Aranesp. We conservatively forecast a lower market share for CERA in Europe relative the U.S. due to greater concern of immunogenicity post Eprex, greater price sensitivity, and a generics

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

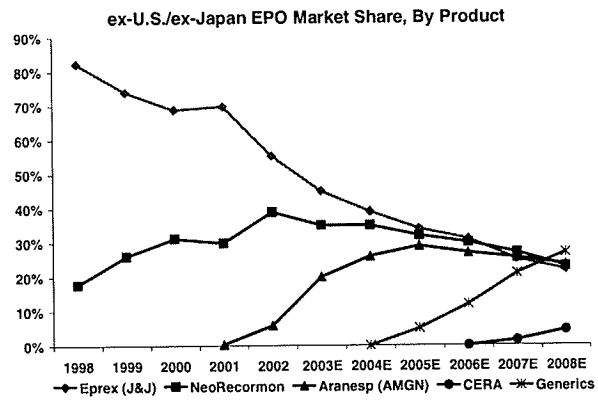
presence in that market in 2005 onwards. **Exhibit 12** outlines our forecast for market share in the ex-U.S./ex-Japan market.

Exhibit 11
**U.S. EPO Market Share: 1998 – 2008E**




Source: Company reports, Bernstein analysis

Exhibit 12
**Ex-U.S., Ex-Japan EPO Market Share: 1998 – 2008E**




Source: Company reports, Bernstein analysis

- **Phase III trials in Europe**. We do not anticipate CERA phase III trials in the U.S. (i.e., trials will likely be conducted in Europe instead). Given the availability of EPO in the U.S., patients are not expected to sign up to be at risk. With Aranesp, there were no phase III trials in the U.S. Instead, two large placebo controlled trials in Europe were the basis for approval. We expect Roche to file using placebo controlled trials conducted in Europe, which we believe are underway now or will begin imminently. We expect these studies will include in the safety and dose response data from the phase II trials in U.S.
  - As with Aranesp, we believe Roche will have to show lack of significant difference from epoetin alfa since the FDA understands that EPO products are similar.
- **Japan launch in 2009.** Our visibility on the Japanese market is currently limited. What we do know is that Japan is already behind the U.S. and Europe in the clinical trials process. As such, we forecast 2009 entry for CERA to the Japanese market. We shall revisit this assumption periodically and adjust our forecasts accordingly.

## Valuation Methodology

### Roche

Our target price for Roche is established from relative price-to-forward earnings data for the European drug group based on the historical relationship of the European and U.S. drug groups as well as the U.S. drug group's relationship to the broader market. Each stock is assigned a premium or discount to the European drug group subsequent to our assessment of fundamentals and news flow/overhang issues. Within our coverage, premiums/(discounts) are as follows: AstraZeneca 25%, Roche 15%, Sanofi-Synthélabo 10%, Novartis (5%), Aventis (30%), and GlaxoSmithKline (30%).

### Amgen

Our biotech valuation methodology builds on our patient based market models for the major product categories. Our models include all currently marketed products, as well as new products and indications in

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

phase III and beyond. We adjust the expected revenues for phase IIb, phase III and pre-approval products to reflect the historical success rate of products at those stages in this group of companies. We currently discount revenues of phase IIb programs by 65%, phase III programs by 35%, post-filing programs by 20% and post-committee programs by 10%.

We value the company's stock by estimating the future sector multiple of rolling twelve month earnings compared to the market (sector relative multiple to market), then estimating the future company multiple relative to the sector (company relative to sector multiple), to calculate an expected company future multiple of earnings. We then apply this multiple to the expected earnings for the following twelve months to calculate a future target price. We cross check this target price by calculating the implied future Price to LTM Sales and Price to LTM R&D expense. Finally, we compare companies across the sector to each other, on a PFE/3 year growth basis, as a final check of our target price.

## Risks

### Roche

Over the next 12 months, Roche will begin reporting Roche Prescription phase II pipeline results and thereafter make go/no-go decisions. Genentech also will report clinical data for multiple products. Positive Genentech and Roche results could provide upside to our view and Roche's valuation; negative results could have an opposite effect. Factors that could affect share strength in the near-term include: further slowing of the hepatitis C market (despite Roche market share gains), earnings volatility related to net financial income, and an increase in provisions related to the vitamins litigation.

### Amgen

The risks to our view of Amgen's outlook are that any of the potential threats to the company's key franchises emerges sooner, or more forcefully, than we expect. Other than the clear risks to Amgen's core erythropoietin franchise posed by CERA and generics outlined above, we see the following additional risks:

- The Neulasta/Neupogen franchise faces the expiry of the key Neupogen patents in the U.S. and E.U. in 2006. The key risk in this franchise is that Amgen is unable to switch the franchise before those dates. We have been conservative in our assumed level of switching, and expect new competition in the U.S. and E.U. beginning in late 2006 or early 2007.
- For both the erythropoietin and filgrastim franchises, material changes in Medicare purchasing could adversely impact pricing freedom, as well as product choice for cancer patients eligible for reimbursement by Medicare. We estimate that up to 2.5% of Amgen's revenue growth could be affected by such changes, although these changes could drain up to 10% of Amgen's revenue growth in 2004 and beyond.
- Any change to the current regulatory approach to generic biologicals would affect Amgen adversely. We believe Amgen has the most exposure of the major biotech companies to biological generics, and if the process were either simplified or expedited, it would negatively affect Amgen's existing revenue base, as well as its top and bottom line growth.

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

## Appendix

Exhibit 13
**Roche Group Consolidated Income Statement, CHF in Millions**

**Roche Group Consolidated Income Statement, CHF in Millions**

| | 2002A | 2003E | 2004E | 2005E | 2006E | 2007E | 2008E | CAGR 02-07 |
|---|---|---|---|---|---|---|---|---|
| Consolidated Sales | 26,546 | 29,183 | 32,894 | 36,926 | 39,760 | 42,818 | 45,840 | 10.0% |
| Cost of Goods Sold | (6,108) | (6,664) | (7,371) | (8,471) | (9,350) | (10,039) | (10,737) | 10.4% |
| **Gross Profit** | 20,438 | 22,518 | 25,523 | 28,455 | 30,410 | 32,779 | 35,103 | 9.9% |
| Marketing & Distribution | (8,127) | (8,920) | (9,275) | (10,145) | (10,338) | (11,073) | (11,857) | 6.4% |
| Research & Development | (4,132) | (4,505) | (5,128) | (6,257) | (6,274) | (6,723) | (7,203) | 10.2% |
| Administration | (1,193) | (1,279) | (1,423) | (1,616) | (1,740) | (1,873) | (2,006) | 9.4% |
| Amortisation of Intangible Assets | (1,502) | (1,519) | (1,646) | (1,780) | (1,878) | (2,022) | (2,164) | 6.1% |
| Impairment of Long-Term Assets | (4) | (4) | (5) | (6) | (6) | (6) | (7) | 10.0% |
| Other Operating Income (Expense), net 1) | (514) | (631) | (489) | (400) | (317) | (245) | (166) | -13.8% |
| **Operating Profit (EBIT)** | 4,966 | 5,660 | 7,556 | 8,250 | 9,856 | 10,835 | 11,701 | 16.9% |
| Net Financial Income (Expense) 2) | 736 | (473) | (309) | 85 | 268 | 395 | 518 | |
| **Profit before Taxes** | 5,701 | 5,187 | 7,247 | 8,335 | 10,124 | 11,231 | 12,218 | 14.5% |
| Income Taxes | (1,674) | (1,504) | (2,102) | (2,334) | (2,784) | (3,032) | (3,299) | |
| **Profit after Taxes** | 4,027 | 3,683 | 5,145 | 6,001 | 7,340 | 8,199 | 8,919 | 15.3% |
| Changes in Accounting Policies | - | - | - | - | - | - | - | |
| Income Applicable to Minority Interests | (182) | (440) | (795) | (1,188) | (1,351) | (1,474) | (1,578) | |
| Share of Result of Associated Companies | (37) | (35) | (37) | (42) | (45) | (48) | (52) | |
| **Net Income** | 3,808 | 3,208 | 4,314 | 4,772 | 5,944 | 6,676 | 7,290 | 11.9% |
| **Basic EPS (Bearer Shares & Non-Voting Equity Securities)** | 4.54 | 3.82 | 5.14 | 5.68 | 7.08 | 7.95 | 8.68 | 11.9% |
| **EPS Growth** | -16.4% | -15.8% | 34.5% | 10.6% | 24.6% | 12.3% | 9.2% | |
| **Elimination of Interest Expense** | (35) | - | - | - | - | - | - | |
| **Increase in Minority Interest** | | | | | | | | |
| **Net Income used for calculation of diluted EPS** | 3,773 | 3,208 | 4,314 | 4,772 | 5,944 | 6,676 | 7,290 | 12.1% |
| **Diluted EPS (Bearer Shares & Non-Voting Equity Securities)** | 4.49 | 3.82 | 5.14 | 5.68 | 7.08 | 7.95 | 8.68 | 12.1% |
| **EPS Growth** | -16.5% | -15.0% | 34.5% | 10.6% | 24.6% | 12.3% | 9.2% | |
| Amortisation of Goodwill | 501 | 585 | 585 | 585 | 585 | 585 | 585 | |
| **Diluted EPS (ex. Goodwill)** | 5.09 | 4.52 | 5.84 | 6.38 | 7.78 | 8.65 | 9.38 | 11.2% |
| EPS Growth | -15.2% | -11.3% | 29.1% | 9.3% | 21.9% | 11.2% | 8.5% | |
| Amortisation of Goodwill in % of Net Income | 13.3% | 18.2% | 13.6% | 12.3% | 9.8% | 8.8% | 8.0% | |

| | 2002A | 2003E | 2004E | 2005E | 2006E | 2007E | 2008E |
|---|---|---|---|---|---|---|---|
| **Margin Analysis as a % of Sales** | | | | | | | |
| Cost of Goods Sold | -23.0% | -22.8% | -22.4% | -22.9% | -23.5% | -23.4% | -23.4% |
| **Gross Profit** | 77.0% | 77.2% | 77.6% | 77.1% | 76.5% | 76.6% | 76.6% |
| Marketing & Distribution | -30.6% | -30.6% | -28.2% | -27.5% | -26.0% | -25.9% | -25.9% |
| Research & Development | -15.6% | -15.4% | -15.6% | -16.9% | -15.8% | -15.7% | -15.7% |
| Administration | -4.5% | -4.4% | -4.3% | -4.4% | -4.4% | -4.4% | -4.4% |
| Amortisation of Intangible Assets | -5.7% | -5.2% | -5.0% | -4.8% | -4.7% | -4.7% | -4.7% |
| Other Operating Income (Expense), net 1) | -1.9% | -2.2% | -1.5% | -1.1% | -0.8% | -0.6% | -0.4% |
| **Operating Profit (EBIT)** | 18.7% | 19.4% | 23.0% | 22.3% | 24.8% | 25.3% | 25.5% |
| Net Financial Income (Expense) 2) | 2.8% | -1.6% | -0.9% | 0.2% | 0.7% | 0.9% | 1.1% |
| Impairment of Financial Assets | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| **Profit before Taxes** | 21.5% | 17.8% | 22.0% | 22.6% | 25.5% | 26.2% | 26.7% |
| Income Taxes | -29.4% | -29.0% | -29.0% | -28.0% | -27.5% | -27.0% | -27.0% |
| **Profit after Taxes** | 15.2% | 12.6% | 15.6% | 16.3% | 18.5% | 19.1% | 19.5% |
| Changes in Accounting Policies | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| Income Applicable to Minority Interests | -0.7% | -1.5% | -2.4% | -3.2% | -3.4% | -3.4% | -3.4% |
| Share of Result of Associated Companies | -0.1% | -0.1% | -0.1% | -0.1% | -0.1% | -0.1% | -0.1% |
| **Net Income** | 14.3% | 11.0% | 13.1% | 12.9% | 15.0% | 15.6% | 15.9% |
| **Depreciation & Amortization (D&A)** | -10.4% | -9.9% | -9.5% | -9.3% | -9.1% | -9.1% | -9.1% |
| Depreciation | -4.7% | -4.7% | -4.7% | -4.7% | -4.7% | -4.7% | -4.7% |
| Amortization | -5.7% | -5.2% | -5.0% | -4.8% | -4.7% | -4.7% | -4.7% |
| **EBITDA** | 29.1% | 29.3% | 32.5% | 31.6% | 33.9% | 34.4% | 34.6% |

Source: Company reports, Bernstein analysis

**Catherine J. Arnold** • arnoldcj@bernstein.com • +1-212-756-1885

Exhibit 14
**Roche Group: Product Revenue Forecasts, CHF in Millions**

| | Annual Projections | | | | | | |
|---|---|---|---|---|---|---|---|
| **Marketed Products** | **2002A** | **2003E** | **2004E** | **2005E** | **2006E** | **2007E** | **2008E** |
| **ONCOLOGY** | | | | | | | |
| MabThera (ex-US)/Rituxan (US) * / ** | 2,332 | 2,849 | 3,339 | 4,369 | 5,060 | 5,978 | 6,842 |
| Herceptin * / ** | 1,007 | 1,232 | 1,413 | 1,546 | 1,656 | 1,748 | 1,830 |
| Neutrogin (Neupogen) ** | 220 | 323 | 329 | 336 | 343 | 350 | 357 |
| Furtulon | 248 | 222 | 200 | 180 | 162 | 146 | 131 |
| Xeloda ** | 444 | 620 | 823 | 1,001 | 1,116 | 1,179 | 1,232 |
| Kytril | 451 | 436 | 443 | 458 | 474 | 490 | 507 |
| **VIROLOGY** | | | | | | | |
| Cymevene/Valcyte | 296 | 275 | 286 | 295 | 304 | 313 | 323 |
| Viracept | 320 | 276 | 268 | 260 | 252 | 244 | 237 |
| Tamiflu ** | 73 | 151 | 164 | 180 | 193 | 204 | 214 |
| Pegasys Franchise | 94 | 753 | 1,070 | 1,265 | 1,336 | 1,393 | 1,446 |
| Copegus | 5 | 200 | 99 | 68 | 42 | 41 | 40 |
| Fuzeon | - | 213 | 592 | 750 | 855 | 870 | 889 |
| **INFECTIOUS DISEASE** | | | | | | | |
| Rocephin | 1,548 | 1,279 | 1,114 | 611 | 268 | 170 | 115 |
| **CENTRAL NERVOUS SYSTEMS** | | | | | | | |
| Lexotan | 244 | 205 | 195 | 187 | 181 | 176 | 171 |
| Madopar | 239 | 230 | 232 | 235 | 235 | 235 | 235 |
| **DERMATOLOGY** | | | | | | | |
| Roaccutane | 911 | 452 | 323 | 258 | 217 | 194 | 178 |
| **CARDIOVASCULAR** | | | | | | | |
| NeoRecormon/Epogin ** | 1,192 | 2,131 | 2,451 | 2,483 | 2,359 | 2,194 | 1,802 |
| Activase/TNKase * | 322 | 300 | 309 | 308 | 302 | 293 | 284 |
| Dilatrend/Coreg | 329 | 401 | 321 | 160 | 104 | 78 | 59 |
| Torem (Demadex) | 216 | 158 | 163 | 168 | 171 | 174 | 176 |
| Inhibace/Inh + | 223 | 217 | 219 | 219 | 213 | 206 | 200 |
| **METABOLISM** | | | | | | | |
| Nutropin/Protropin * | 477 | 445 | 446 | 417 | 375 | 330 | 288 |
| Xenical | 763 | 646 | 622 | 605 | 596 | 590 | 584 |
| **INFLAMMATION / IMMUNOMODULATION** | | | | | | | |
| CellCept ** | 1,173 | 1,322 | 1,394 | 1,457 | 1,508 | 1,549 | 1,587 |
| **BRONCHOPULMONARY** | | | | | | | |
| Pulmozyme * | 320 | 356 | 397 | 428 | 451 | 466 | 478 |
| All Other | 4,307 | 4,157 | 3,743 | 3,631 | 3,522 | 3,416 | 3,314 |
| **Total Marketed** | **17,754** | **19,849** | **20,955** | **21,876** | **22,293** | **23,027** | **23,517** |
| **Growth** | **3.2%** | **11.8%** | **5.6%** | **4.4%** | **1.9%** | **3.3%** | **2.1%** |
| **Pipeline Products** | **2002A** | **2003E** | **2004E** | **2005E** | **2006E** | **2007E** | **2008E** |
| **ONCOLOGY** | | | | | | | |
| Bondronate | - | 32 | 80 | 124 | 167 | 193 | 212 |
| Tarceva * | - | - | - | 129 | 198 | 248 | 296 |
| Avastin *** | - | - | 1,288 | 2,850 | 3,584 | 4,105 | 4,321 |
| Pemtumomab **** | - | - | - | 48 | 83 | 107 | 122 |
| CERA (R744) | - | - | - | - | - | 341 | 1,222 |
| R1273 * - solid tumors (monoclonal) | - | - | - | - | - | 20 | 127 |
| R1124 - emesis (GPCR modulator) | - | - | - | - | 40 | 76 | 127 |
| **VIROLOGY** | | | | | | | |
| R724 (Fuzeon 2nd Gen) | - | - | - | - | - | 40 | 80 |
| **DERMATOLOGY** | | | | | | | |
| Raptiva*** | - | 12 | 135 | 254 | 340 | 584 | 703 |
| **METABOLISM** | | | | | | | |
| Boniva | - | - | - | 45 | 96 | 166 | 215 |
| **INFLAMMATION / IMMUNOMODULATION** | | | | | | | |
| MRA ** | - | - | - | - | - | 75 | 175 |
| **BRONCHOPULMONARY** | | | | | | | |
| Xolair *** | - | 29 | 263 | 675 | 1,034 | 1,083 | 1,048 |
| **DIABETES** | | | | | | | |
| R483 (insulin sensitizer) | - | - | - | - | - | 25 | 50 |
| **CENTRAL NERVOUS SYSTEMS** | | | | | | | |
| R450 (Urin Incont) | - | - | - | - | 40 | 80 | 133 |
| **IMMUNOLOGICAL DISEASE** | | | | | | | |
| LDP-02 Antibody (inflammatory bowel) | - | - | - | - | - | - | - |
| rhuFab V2 (AMD) | - | - | - | - | 71 | 145 | 265 |
| **Total Pipeline** | **-** | **73** | **1,766** | **4,126** | **5,654** | **7,288** | **9,094** |
| **Growth** | **-** | **NM** | **NM** | **133.6%** | **37.0%** | **28.9%** | **24.8%** |
| **Total Pharmaceutical Sales Incl. Genentch & Chugal** | **17,754** | **19,922** | **22,721** | **26,002** | **27,947** | **30,315** | **32,611** |
| **Growth** | **3.2%** | **12.2%** | **14.0%** | **14.4%** | **7.5%** | **8.5%** | **7.6%** |

Source: Company reports, Bernstein analysis

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

Exhibit 15
**Amgen Income Statement, $ in Millions**

| | 2002 | 1Q03A | 2Q03E | 3Q03 | 4Q03 | 2003 | 1Q04 | 2Q04 | 3Q04 | 4Q04 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Revenues: | | | | | | | | | | | | | | | |
| Product sales | $4,991.2 | $1,635.9 | $1,916.5 | $2,044.2 | $2,241.4 | $7,838.0 | $2,198.0 | $2,370.6 | $2,424.6 | $2,574.6 | $9,567.7 | $11,050.7 | $12,342.5 | $13,460.2 | $14,142.9 |
| Other revenue | 531.8 | 125.3 | 124.6 | 142.0 | 134.9 | 526.8 | 120.3 | 119.6 | 135.1 | 128.5 | 503.5 | 478.9 | 451.7 | 423.8 | 396.8 |
| **Total revenues** | **5,523.0** | **1,761.2** | **2,041.1** | **2,186.2** | **2,376.3** | **8,364.8** | **2,318.3** | **2,490.1** | **2,559.7** | **2,703.1** | **10,071.2** | **11,529.6** | **12,794.2** | **13,884.1** | **14,539.6** |
| Expenses: | | | | | | | | | | | | | | | |
| Cost of sales | 689.5 | 278.4 | 324.2 | 346.1 | 374.6 | 1,323.3 | 354.8 | 370.9 | 386.9 | 406.4 | 1,518.9 | 1,713.0 | 1,920.7 | 2,101.3 | 2,242.5 |
| R&D | 1,098.5 | 341.6 | 384.6 | 420.8 | 475.3 | 1,622.3 | 452.1 | 482.2 | 492.5 | 517.0 | 1,943.7 | 2,177.8 | 2,380.7 | 2,556.8 | 2,658.4 |
| SG&A | 1,317.5 | 303.1 | 358.6 | 393.5 | 439.6 | 1,494.8 | 417.3 | 448.2 | 460.7 | 486.6 | 1,812.8 | 2,075.3 | 2,303.0 | 2,499.1 | 2,617.1 |
| Revenue Sharing (Estimated) | 108.6 | 82.2 | 91.2 | 103.5 | 109.5 | 386.4 | 111.0 | 109.4 | 122.1 | 125.9 | 468.5 | 590.4 | 680.1 | 750.8 | 807.6 |
| Other expenses | (12.6) | (9.6) | (12.3) | (3.7) | (6.3) | (31.9) | (10.4) | (13.3) | (4.0) | (6.8) | (34.5) | (36.9) | (39.1) | (41.4) | (42.0) |
| Total expenses (excluding rev sharing/incl. in SG | 3,201.5 | 995.7 | 1,146.3 | 1,260.3 | 1,392.6 | 4,794.9 | 1,324.7 | 1,397.4 | 1,458.3 | 1,529.1 | 5,709.5 | 6,519.7 | 7,245.3 | 7,866.7 | 8,283.6 |
| Operating income (EBIT) | 2,321.5 | 765.5 | 894.8 | 925.9 | 983.7 | 3,569.9 | 993.6 | 1,092.7 | 1,101.5 | 1,174.0 | 4,361.7 | 5,009.9 | 5,548.9 | 6,017.3 | 6,256.0 |
| Nonoperating income (interest), net | 100.0 | 25.9 | 31.6 | 33.4 | 34.0 | 124.9 | 41.5 | 43.0 | 47.6 | 49.5 | 181.5 | 248.8 | 334.8 | 437.8 | 545.8 |
| Pre-tax income | 2,421.5 | 791.4 | 926.4 | 959.4 | 1,017.7 | 3,694.8 | 1,035.1 | 1,135.7 | 1,149.0 | 1,223.4 | 4,543.3 | 5,258.7 | 5,883.8 | 6,455.2 | 6,801.8 |
| Tax | 746.6 | 233.5 | 273.3 | 292.6 | 310.4 | 1,109.8 | 315.7 | 344.0 | 345.9 | 366.4 | 1,371.9 | 1,559.0 | 1,726.9 | 1,884.2 | 1,979.5 |
| **Net income (excluding charges)** | **$1,674.9** | **$557.9** | **$653.1** | **$666.8** | **$707.3** | **$2,585.0** | **$719.4** | **$791.8** | **$803.2** | **$857.1** | **$3,171.4** | **$3,699.7** | **$4,156.9** | **$4,571.0** | **$4,822.4** |
| Earnings per share (basic): | $1.45 | $0.43 | $0.51 | $0.51 | $0.54 | $1.99 | $0.55 | $0.61 | $0.62 | $0.66 | $2.43 | $2.85 | $3.21 | $3.55 | $3.75 |
| **Earnings per share (diluted):** | **$1.39** | **$0.42** | **$0.48** | **$0.49** | **$0.52** | **$1.92** | **$0.53** | **$0.59** | **$0.60** | **$0.64** | **$2.35** | **$2.78** | **$3.13** | **$3.45** | **$3.66** |
| Dividend per share | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Weighted ave. shares (basic): | 1,153.5 | 1,290.5 | 1,287.9 | 1,299.9 | 1,304.4 | 1,297.6 | 1,306.0 | 1,304.8 | 1,303.6 | 1,302.4 | 1,304.2 | 1,299.4 | 1,294.4 | 1,289.3 | 1,284.4 |
| Weighted ave. shares (diluted): | 1,209.9 | 1,349.9 | 1,347.0 | 1,348.8 | 1,358.5 | 1,344.0 | 1,359.6 | 1,352.1 | 1,344.7 | 1,337.2 | 1,348.4 | 1,332.1 | 1,328.4 | 1,324.7 | 1,319.2 |
| Adjustments to GAAP: | | | | | | | | | | | | | | | |
| One-time adjustments to GAAP (pre-tax) | (4,461.2) | (91.6) | (65.1) | - | - | - | - | - | - | - | - | - | - | - | - |
| One-time adjustments to GAAP (after-tax) | (3,175.4) | (64.6) | (45.9) | - | - | - | - | - | - | - | - | - | - | - | - |
| GAAP net income | (1,391.9) | 493.3 | 607.2 | - | - | - | - | - | - | - | - | - | - | - | - |
| GAAP EPS basic | ($1.21) | $0.38 | $0.47 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 |
| GAAP EPS diluted | ($1.15) | $0.37 | $0.45 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 | $0.00 |
| **MARGIN ANALYSIS:** | | | | | | | | | | | | | | | |
| Gross margin (1-COGS/product sales) | 86.2% | 83.0% | 83.1% | 83.1% | 83.3% | 83.1% | 83.9% | 84.4% | 84.0% | 84.2% | 84.1% | 84.5% | 84.4% | 84.4% | 84.1% |
| R&D to total revenue | 19.9% | 19.4% | 18.8% | 19.3% | 20.0% | 19.4% | 19.5% | 19.4% | 19.2% | 19.1% | 19.3% | 18.9% | 18.6% | 18.4% | 18.3% |
| SG&A to total revenue (excl profit share) | 23.9% | 17.2% | 17.6% | 18.0% | 18.5% | 17.9% | 18.0% | 18.0% | 18.0% | 18.0% | 18.0% | 18.0% | 18.0% | 18.0% | 18.0% |
| Profit share to total revenue | 2.0% | 4.7% | 4.5% | 4.7% | 4.6% | 4.6% | 4.8% | 4.4% | 4.8% | 4.7% | 4.7% | 5.1% | 5.3% | 5.4% | 5.6% |
| Operating margin (EBIT/product sales) | 46.5% | 46.8% | 46.7% | 45.3% | 43.9% | 45.5% | 45.2% | 46.1% | 45.4% | 45.6% | 45.6% | 45.3% | 45.0% | 44.7% | 44.2% |
| Nonoperating (nonoperating/sales) | 2.0% | 1.6% | 1.6% | 1.6% | 1.5% | 1.6% | 1.9% | 1.8% | 2.0% | 1.9% | 1.9% | 2.3% | 2.7% | 3.3% | 3.9% |
| Pretax margin (pretax income/product sales) | 48.5% | 48.4% | 48.3% | 46.9% | 45.4% | 47.1% | 47.1% | 47.9% | 47.4% | 47.5% | 47.5% | 47.6% | 47.7% | 48.0% | 48.1% |
| Effective tax rate | 30.8% | 29.5% | 29.5% | 30.5% | 30.5% | 30.0% | 30.5% | 30.3% | 30.1% | 29.9% | 30.2% | 29.6% | 29.3% | 29.2% | 29.1% |
| Net margin (net income/sales) | 30.3% | 31.7% | 32.0% | 30.5% | 29.8% | 30.9% | 31.0% | 31.8% | 31.4% | 31.7% | 31.5% | 32.1% | 32.5% | 32.9% | 33.2% |
| **ANNUAL GROWTH** | | | | | | | | | | | | | | | |
| Total product sales | 42.2% | 80.0% | 71.9% | 51.9% | 38.2% | 57.0% | 34.4% | 23.7% | 18.6% | 14.9% | 22.1% | 15.5% | 11.7% | 9.1% | 5.1% |
| Other revenue | 5.4% | 25.4% | -6.9% | -7.5% | -6.7% | -0.9% | -4.0% | -4.0% | -4.8% | -4.7% | -4.4% | -4.9% | -5.7% | -6.2% | -6.4% |
| Total revenues | 37.5% | 74.6% | 63.4% | 45.8% | 34.6% | 51.5% | 31.6% | 22.0% | 17.1% | 13.8% | 20.4% | 14.5% | 11.0% | 8.5% | 4.7% |
| Cost of sales | 70.9% | 168.7% | 145.8% | 72.4% | 47.9% | 91.9% | 27.4% | 14.4% | 11.8% | 8.5% | 14.8% | 12.8% | 12.1% | 9.4% | 6.7% |
| Research & development | 27.0% | 67.9% | 64.6% | 38.4% | 33.0% | 47.7% | 32.3% | 25.4% | 17.0% | 8.8% | 19.8% | 12.0% | 9.3% | 7.4% | 4.0% |
| SG&A | 35.7% | 23.3% | 11.9% | 19.4% | 4.2% | 13.5% | 37.7% | 25.0% | 17.1% | 10.7% | 21.3% | 14.5% | 11.0% | 8.5% | 4.7% |
| Operating expenses | 42.8% | 80.7% | 67.5% | 51.7% | 35.7% | 49.8% | 33.0% | 21.9% | 15.7% | 9.8% | 19.1% | 14.2% | 11.1% | 8.6% | 5.3% |
| Operating income | 30.9% | 67.4% | 58.4% | 38.5% | 33.0% | 53.8% | 29.8% | 22.1% | 19.0% | 19.3% | 22.2% | 14.9% | 10.8% | 8.4% | 4.0% |
| Other income | -35.5% | -29.4% | -3.7% | 176.1% | 84.9% | 24.9% | 60.2% | 36.0% | 42.4% | 45.4% | 45.3% | 37.1% | 34.6% | 30.8% | 24.7% |
| Earnings before income taxes | 25.5% | 60.2% | 55.0% | 41.0% | 34.3% | 52.6% | 30.8% | 22.6% | 19.8% | 20.2% | 23.0% | 15.7% | 11.9% | 9.7% | 5.4% |
| Taxes | 14.5% | 52.4% | 47.6% | 49.1% | 46.5% | 48.6% | 35.2% | 25.9% | 18.2% | 18.0% | 23.6% | 13.6% | 10.8% | 9.1% | 5.1% |
| Net income | 31.2% | 63.7% | 58.4% | 37.7% | 29.5% | 54.3% | 28.9% | 21.2% | 20.5% | 21.2% | 22.7% | 16.7% | 12.4% | 10.0% | 5.5% |
| EPS (diluted) | 18.0% | 31.3% | 29.2% | 33.0% | 28.5% | 38.4% | 26.0% | 20.8% | 20.8% | 23.1% | 22.3% | 18.1% | 12.7% | 10.3% | 5.9% |
| Gross margin | -2.6% | -6.3% | -5.8% | -2.4% | -1.3% | -3.6% | 1.1% | 1.5% | 1.2% | 1.1% | 1.2% | 0.4% | -0.1% | -0.1% | -0.3% |
| Operating margin | -7.9% | -7.0% | -7.8% | -8.8% | -3.8% | -2.1% | -3.4% | -1.3% | 0.3% | 3.9% | 0.1% | -0.6% | -0.8% | -0.6% | -1.1% |
| Net margin | -4.6% | -6.3% | -3.1% | -5.6% | -3.7% | 1.9% | -2.0% | -0.6% | 2.9% | 6.5% | 1.9% | 1.9% | 1.3% | 1.3% | 0.7% |

Source: Company reports, Bernstein analysis

Catherine J. Arnold • arnoldcj@bernstein.com • +1-212-756-1885

Exhibit 16
**Amgen Product Revenue Forecasts**

| | 2002 | 1Q03A | 2Q03E | 3Q03 | 4Q03 | 2003E | 1Q04 | 2Q04 | 3Q04 | 4Q04 | 2004E | 2005E | 2006E | 2007E | 2008E |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SALES | | | | | | | | | | | | | | | |
| EXISTING PRODUCTS | | | | | | | | | | | | | | | |
| Epogen | $2,260.9 | $547.0 | $611.1 | $608.7 | $673.0 | $2,439.8 | $593.5 | $660.7 | $655.9 | $723.2 | $2,633.3 | $2,813.2 | $2,986.0 | $3,156.7 | $3,185.3 |
| Aranesp | 415.9 | 254.8 | 347.7 | 429.6 | 494.0 | 1,526.1 | 535.1 | 556.3 | 569.2 | 592.8 | 2,253.4 | 2,638.9 | 2,995.9 | 3,408.6 | 3,666.2 |
| Erythropoietin franchise | 2,676.8 | 801.8 | 958.8 | 1,038.2 | 1,167.1 | 3,965.9 | 1,128.6 | 1,217.0 | 1,225.1 | 1,316.1 | 4,886.8 | 5,452.2 | 5,981.9 | 6,565.3 | 6,851.6 |
| Neupogen | 1,379.6 | 284.0 | 330.2 | 300.9 | 297.2 | 1,212.3 | 255.8 | 296.8 | 269.9 | 266.0 | 1,088.5 | 970.7 | 861.7 | 762.7 | 673.7 |
| Neulasta | 463.5 | 257.9 | 303.5 | 340.1 | 392.2 | 1,293.7 | 425.5 | 472.6 | 502.5 | 552.7 | 1,953.4 | 2,456.4 | 2,800.0 | 3,012.1 | 3,135.6 |
| Filgrastim franchise | 1,843.1 | 541.9 | 633.7 | 641.0 | 689.4 | 2,505.9 | 681.4 | 769.4 | 772.4 | 818.8 | 3,041.9 | 3,427.1 | 3,661.7 | 3,774.8 | 3,809.3 |
| Enbrel | 362.1 | 274.0 | 304.0 | 345.0 | 365.0 | 1,288.0 | 369.9 | 364.8 | 407.1 | 419.8 | 1,561.6 | 1,902.9 | 2,115.4 | 2,242.5 | 2,307.7 |
| Kineret | 108.5 | 18.1 | 19.4 | 20.0 | 20.0 | 77.5 | 18.1 | 19.4 | 20.0 | 20.0 | 77.5 | 77.5 | 77.5 | 77.5 | 77.5 |
| Other | 0.7 | 0.1 | 0.6 | - | - | 0.7 | - | - | - | - | - | - | - | - | - |
| Total product sales - existing products | 4,991.2 | 1,635.9 | 1,916.5 | 2,044.2 | 2,241.4 | 7,838.0 | 2,198.0 | 2,370.6 | 2,424.6 | 2,574.6 | 9,567.7 | 10,859.7 | 11,836.5 | 12,660.1 | 13,046.0 |
| FUTURE PRODUCTS* | | | | | | | | | | | | | | | |
| ABX-EGF | - | - | - | - | - | - | - | - | - | - | - | - | 56.3 | 172.5 | 242.0 |
| POS adj. | - | - | - | - | - | - | - | - | - | - | - | - | 19.7 | 60.4 | 84.7 |
| Epratuzumab | - | - | - | - | - | - | - | - | - | - | - | - | 112.5 | 235.4 | 398.5 |
| POS adj. | - | - | - | - | - | - | - | - | - | - | - | - | 39.4 | 82.4 | 139.5 |
| Cinacalcet | - | - | - | - | - | - | - | - | - | - | - | 203.8 | 360.3 | 547.3 | 777.8 |
| POS adj. | - | - | - | - | - | - | - | - | - | - | - | 163.0 | 288.2 | 437.9 | 622.3 |
| KGF | - | - | - | - | - | - | - | - | - | - | - | 40.0 | 226.7 | 313.5 | 357.8 |
| POS adj. | - | - | - | - | - | - | - | - | - | - | - | 28.0 | 158.7 | 219.5 | 250.5 |
| Total product sales - new products | - | - | - | - | - | - | - | - | - | - | - | 243.8 | 755.7 | 1,268.7 | 1,776.1 |
| Total product sales - new products POS adj. | - | - | - | - | - | - | - | - | - | - | - | 191.0 | 506.0 | 800.1 | 1,096.9 |
| OTHER REVENUE | | | | | | | | | | | | | | | |
| Corporate partner revenues | 200.3 | 33.9 | 32.7 | 42.2 | 37.9 | 146.7 | 26.2 | 26.5 | 35.5 | 32.9 | 121.1 | 111.0 | 106.6 | 104.5 | 103.5 |
| Royalty income | 331.5 | 91.4 | 91.9 | 99.8 | 97.0 | 380.1 | 94.1 | 93.1 | 99.6 | 95.6 | 382.4 | 367.9 | 345.2 | 319.3 | 293.2 |
| Total revenues - existing products | 5,523.0 | 1,761.2 | 2,041.1 | 2,186.2 | 2,376.3 | 8,364.8 | 2,318.3 | 2,490.1 | 2,559.7 | 2,703.1 | 10,071.2 | 11,338.6 | 12,288.3 | 13,084.0 | 13,442.8 |
| Total revenues - existing & new products POS adj. | 5,523.0 | 1,761.2 | 2,041.1 | 2,186.2 | 2,376.3 | 8,364.8 | 2,318.3 | 2,490.1 | 2,559.7 | 2,703.1 | 10,071.2 | 11,529.6 | 12,794.2 | 13,884.1 | 14,539.6 |
| ANNUAL GROWTH | | | | | | | | | | | | | | | |
| EXISTING PRODUCTS | | | | | | | | | | | | | | | |
| Epogen | 7% | 7% | 7% | 9% | 9% | 8% | 9% | 8% | 8% | 7% | 8% | 7% | 6% | 6% | 1% |
| Aranesp | N/A | 550% | 521% | 278% | 139% | 267% | 110% | 60% | 33% | 20% | 48% | 17% | 14% | 14% | 8% |
| Erythropoietin franchise | 26% | 45% | 53% | 48% | 44% | 48% | 40% | 37% | 34% | 31% | 23% | 12% | 10% | 10% | 4% |
| Neupogen | 2% | -20% | -9% | -9% | -10% | -12% | -10% | -10% | -10% | -10% | -10% | -11% | -11% | -11% | -12% |
| Neulasta | N/A | N/A | 176% | 140% | 85% | 179% | 65% | 56% | 48% | 41% | 51% | 26% | 14% | 8% | 4% |
| Filgrastim franchise | 37% | 53% | 34% | 31% | 28% | 36% | 26% | 24% | 22% | 20% | 21% | 13% | 7% | 3% | 1% |
| Enbrel | N/A | N/A | N/A | 118% | 79% | 256% | 35% | 20% | 18% | 15% | 21% | 22% | 11% | 6% | 3% |
| Kineret | N/A | N/A | N/A | N/A | 0% | -29% | 0% | 0% | 0% | 0% | 0% | 0% | 0% | 0% | 0% |
| Other | -98% | nm | na | na | na | na | na | na | na | na | na | na | na | na | na |
| Total product sales - existing products | 42% | 80% | 72% | 52% | 38% | 57% | 34% | 24% | 19% | 15% | 22% | 14% | 9% | 7% | 3% |
| FUTURE PRODUCTS | | | | | | | | | | | | | | | |
| ABX-EGF | | | | | | | | | | | | | N/A | 207% | 40% |
| Epratuzumab | | | | | | | | | | | | N/A | #DIV/0! | 109% | 69% |
| Cinacalcet | | | | | | | | | | | | N/A | 77% | 52% | 42% |
| KGF | | | | | | | | | | | | N/A | 467% | 38% | 14% |
| Total product sales - new products | | | | | | | | | | | N/A | #DIV/0! | 165% | 58% | 37% |
| Total product sales - new products POS adjusted | | | | | | | | | | | N/A | #DIV/0! | 165% | 58% | 37% |
| OTHER REVENUE | | | | | | | | | | | | | | | |
| Corporate partner revenues | -21% | 8% | -39% | -33% | -27% | -27% | -23% | -19% | -16% | -13% | -17% | -8% | -4% | -2% | -1% |
| Royalty income | 31% | 34% | 15% | 10% | 5% | 15% | 3% | 1% | 0% | -1% | 1% | -4% | -6% | -7% | -8% |
| Total revenues - existing products | 38% | 75% | 63% | 46% | 35% | 51% | 32% | 22% | 17% | 14% | 20% | 13% | 8% | 6% | 3% |
| Total revenues - existing & new products POS adj. | 38% | 75% | 63% | 46% | 35% | 51% | 32% | 22% | 17% | 14% | 20% | 14% | 11% | 9% | 5% |

Source: Company reports, Bernstein analysis

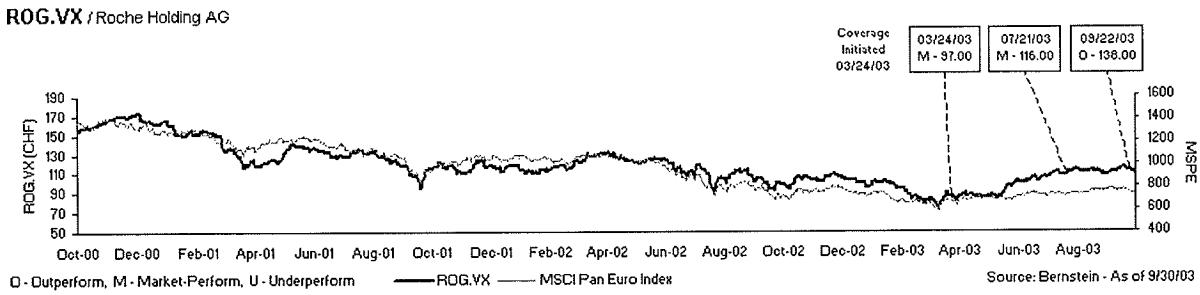
## CERTIFICATIONS AND DISCLOSURES

- Bernstein analysts are compensated based on aggregate contributions to the research franchise as measured by account penetration, productivity and proactivity of investment ideas. No analysts are compensated based on performance in, or contributions to, generating investment banking revenues.
- Bernstein rates stocks based on forecasts of relative performance for the next 6-12 months versus the S&P 500 for U.S. listed stocks and versus the MSCI Pan Europe Index for stocks listed on the European exchanges — unless otherwise specified. We have three categories of ratings:

  Outperform: Stock will outpace the market index by more than 15 pp in the year ahead.

  Market-Perform: Stock will perform in line with the market index to within +/-15 pp in the year ahead.

  Underperform: Stock will trail the performance of the market index by more than 15 pp in the year ahead.
- Bernstein currently makes or plans to make a market in every NASDAQ security contained within our coverage universe.
- CERTIFICATION: I, Catherine J. Arnold, certify that all of the views expressed in my report accurately reflect my personal views about any and all of the subject securities or issuers and that no part of my compensation was, is, or will be, directly or indirectly, related to the specific recommendations or views in this report.
- Andrea Hotz maintains positions in Eli Lilly & Co. (LLY) and Berkshire Hathaway.
- CERTIFICATION: I, Geoffrey Porges, certify that all of the views expressed in my report accurately reflect my personal views about any and all of the subject securities or issuers and that no part of my compensation was, is, or will be, directly or indirectly, related to the specific recommendations or views in this report.
- Dr Porges, as a former non-executive director of the UK specialty vaccine company Acambis plc, owns a common equity position in ACAM.
- One or more of the officers, directors, members or employees of Sanford C. Bernstein & Co., LLC, Sanford C. Bernstein Limited and/or its affiliates may at any time hold, increase or decrease positions in securities of any company mentioned herein.
- Sanford C. Bernstein & Co., LLC, Sanford C. Bernstein Limited, or its or their affiliates may provide investment management or other services for such companies or employees of such companies or their pension or profit sharing plans, and may give advice to others as to investments in such companies. These entities may effect transactions that are similar to or different from those mentioned herein.




### Bernstein Distribution of Ratings

| | |
|---|---|
| Outperform | 46.0% |
| Market-Perform | 45.6% |
| Underperform | 8.5% |

Source: Bernstein - As of 09/30/03

Approved By: JAG