

# First-In-Class Oral Calcimimetic Shown To Reduce Parathyroid Hormone Levels In Chronic Kidney Disease

## November 3, 2002

PHILADELPHIA, PA, November 3, 2002 - Amgen (Nasdaq: AMGN), the world's largest biotechnology company, today announced phase 2 data for Amgen's investigational compound AMG 073 (cinacalcet HCl) suggesting that AMG 073 can reduce and maintain parathyroid hormone (PTH) levels within the target range in end stage renal disease (ESRD) patients with secondary hyperparathyroidism (HPT). Elevated PTH is associated with bone pain, fractures, and increased mortality risk. The data was presented at the 35th annual meeting of the American Society of Nephrology (ASN).

Data were also presented that suggest that AMG 073 may also reduce the frequency of self-reported cognitive problems (such as confusion, difficulty thinking, and forgetfulness) in patients with secondary HPT. The improvement seen in the AMG 073 group was due, at least in part, to reductions in PTH.

### Achieving Target PTH Levels

The study was a randomized, placebo-controlled, double-blind, 12-week trial. AMG 073 was given at doses up to 180 mg to 82 hemodialysis patients with pre-study PTH levels >300 pg/mL -- a high level -- despite receiving standard therapy. AMG 073 reduced PTH to the target level in 54% of patients who were not controlled on current therapy. Concomitant vitamin D and phosphate binder use was similar between treatment groups. AMG 073 was well-tolerated and adverse events were similar in the two treatment groups.

"AMG 073 reduced PTH levels to the target range in the majority of these patients who were not previously controlled with standard care," said Dr. Block. "These results demonstrate the potential benefit of AMG 073 as a novel therapy for the chronic treatment of secondary hyperparathyroidism. Because AMG 073 appears to reduce PTH without increasing Ca x P levels, it may offer advantages over current therapies." [ASN poster # SU-P0509; Block, et al]

### **Promising New Class and Compound**

AMG 073 is the first compound in the Calcimimetics drug class. Calcimimetic compounds bind to and modulate the calcium-sensing receptors on the parathyroid gland, increasing sensitivity of the receptors to calcium levels in the bloodstream, which leads to a rapid reduction in PTH secretion from the gland. Calcimimetic agents, such as AMG 073, may provide therapeutic benefits in controlling PTH and ameliorating bone disease without increasing Ca x P levels. The current standard of care for these patients typically includes vitamin D sterols, which can result in interruptions of vitamin D therapy, and elevations of blood calcium and/or phosphorus levels.

Phase 3 trials for AMG 073 were launched December 2001.

### Other AMG 073 Studies Presented at ASN

## Two-Year Treatment with Calcimimetic AMG 073 in Hemodialysis Patients with Secondary Hyperparathyroidism

Another study presented at the conference supports the benefit of long-term calcimimetic administration in addition to standard therapy. At the end of one year of treatment, 50 percent of AMG 073 patients had a 30 percent or greater reduction in PTH from baseline levels, compared to 12 percent of placebo patients. After this one-year study period, patients continued receiving AMG 073 for a second year. After two years total study duration, 55 percent of AMG 073 patients had a 30 percent or greater reduction in PTH. AMG 073 treatment also prevented Ca x P levels from increasing over two years of treatment. Elevated Ca x P levels have been linked to increased risk of cardiovascular complications and death. [ASN poster #SU-P0508; Moe, et al.]

Self-Reported Cognitive Functioning in Hemodialysis Patients with Secondary Hyperparathyroidism: The Effect of the Calcimimetic AMG 073 Prior research in animal models and humans suggests that high levels of PTH may impair cognitive function in patients with secondary HPT. Reducing and maintaining target levels of PTH may lower the frequency of self-reported cognitive problems (e.g., confusion, difficulty thinking, forgetfulness, etc.) in patients with secondary HPT. This pooled analysis of two phase 2 studies suggests that the frequency of self-reported cognitive problems may be reduced with AMG 073, as compared to placebo, at least in part due to reductions in PTH. Larger controlled studies are needed to further clarify these findings. [ASN poster #SU-P0800; Chertow, et al.]

The Effects of One-Year Treatment with the Calciminetic AMG 073 on Bone Health in ESRD Patients with Secondary Hyperparathyroidism In this study, no deleterious effects on bone histology were seen in patients receiving AMG 073 for one year. The observed trends toward improving bone histology in the small number of patients studied who received AMG 073 will need to be confirmed in larger studies. These findings suggest a potential benefit of AMG 073 on bone disease in patients with ESRD. [ASN poster #: SU-P0510; Quarles, et al.]

#### Amgen Background

AMG 073 (cinacalcet HCl) is a pipeline product from Amgen, the company that revolutionized anemia treatment with the discovery of recombinant erythropoietin, which is currently marketed by Amgen as EPOGEN® and by Johnson & Johnson as Procrit®.

Amgen also developed Aranesp® (darbepoetin alfa) which provided another option in anemia treatment that resulted in a unique molecule with an approximately three times longer half-life and greater biological activity than Epoetin alfa with the added benefit of less-frequent dosing schedules, while also retaining a similar safety profile.

Amgen is a global biotechnology company that discovers, develops, manufactures and markets important human therapeutics based on advances in cellular and molecular biology.

This news release contains forward-looking statements that involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission reports filed by Amgen, including our most recent Form 10-Q. Amgen conducts research in the

biotechnology/pharmaceutical field where movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate will be successful and become a commercial product.

Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. In addition, sales of our products are affected by reimbursement policies imposed by third party payors, including governments, private insurance plans and managed care providers. These government regulations and reimbursement policies may affect the development, usage and pricing of our products.

In addition, while Amgen routinely obtains patents for our products and technology, the protection offered by Amgen patents and patent applications may be challenged, invalidated or circumvented by our competitors.

Because forward-looking statements involve risks and uncertainties, actual results may differ materially from current results expected by Amgen. Amgen is providing this information as of November 3, 2002 and expressly disclaims any duty to update information contained in this press release.

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