First Head-to-Head Trial of a TNF Inhibitor Versus Methotrexate Monotherapy in Psoriatic Arthritis Shows ENBREL® (Etanercept) Monotherapy and Combination Therapy Both Superior to Methotrexate

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Results From Head-To-Head Phase 3 SEAM-PsA Study Assessing ENBREL and Methotrexate Regimens in Patients With Psoriatic Arthritis Presented at 2018 ACR/ARHP Annual Meeting

Additional Phase 3b Results Show Modified ENBREL Formulation Associated With Significantly Lower Mean Injection Site Pain Versus Prior Formulation

Data Presentations Result of Continued Dedication to Evaluate Optimal Use of ENBREL

THOUSAND OAKS, Calif., Oct. 24, 2018 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that positive results from the Phase 3 SEAM-PsA study comparing the efficacy of Enbrel® (etanercept) monotherapy and ENBREL plus methotrexate to methotrexate monotherapy in patients with psoriatic arthritis (PsA) were presented in a late-breaking poster session at the 2018 American College of Rheumatology (ACR)/Association of Rheumatology Health Professionals (ARHP) Annual Meeting in Chicago, Oct. 19-24, 2018.

This study was undertaken to address key knowledge gaps regarding the optimal use of methotrexate and TNF inhibitors such as ENBREL in patients with early disease who have not previously received treatment with biologics and methotrexate for PsA. Results showed that a significantly higher proportion of patients on ENBREL monotherapy and on combination therapy achieved the primary endpoint of ACR 20 response compared with patients on methotrexate monotherapy (60.9 percent [*p*=0.029] and 65.0 percent [*p*=0.005] versus 50.7 percent, respectively). A significantly higher proportion of patients on ENBREL monotherapy and on combination therapy also achieved Minimal Disease Activity (MDA), a PsA-specific composite measure and a key secondary endpoint, compared with patients on methotrexate monotherapy (35.9 percent [*p*=0.005] and 35.7 percent [*p*=0.005] versus 22.9 percent, respectively).

Patients on ENBREL monotherapy and on combination therapy also had greater responses on additional secondary endpoints of ACR 50 and ACR 70 compared with patients on methotrexate monotherapy (ACR 50: 44.4 percent (*p*=0.006), 45.7 percent (*p*<0.001) versus 30.6 percent; ACR 70: 29.2 percent (*p*<0.001), 27.7 percent (*p*<0.001) versus 13.8 percent [*p* values are unadjusted]). Overall, while not evaluated in prespecified analyses, the results of adding methotrexate to ENBREL in combination therapy were similar to the results with ENBREL monotherapy, with the exception of some differences in skin-related endpoints.

"The SEAM-PsA trial results suggest that methotrexate is generally efficacious in treating psoriatic arthritis symptoms in patients with early disease. ENBREL monotherapy has greater efficacy compared with methotrexate as monotherapy across key measures of psoriatic arthritis activity. While not formally tested, ENBREL monotherapy and combination therapy have generally similar efficacy," said Philip Mease, M.D., lead SEAM-PsA investigator and study author, Swedish Medical Center and University of Washington. "These results provide information of practical value for psoriatic arthritis patients and their physicians to optimally manage the disease while addressing potential challenges associated with combination therapy."

"First approved 20 years ago for moderate–to-severe rheumatoid arthritis, ENBREL has a long history in helping patients with inflammatory diseases, such as psoriatic arthritis, manage their condition," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "We believe it is critical to continuously explore how we can improve patient care with our medicines, as shown by the present study, examining the optimal use of our therapy to treat this serious and chronic disease; our newest administration device, the ENBREL Mini® single dose prefilled cartridge with AutoTouch® reusable autoinjector designed with patient ergonomics in mind; and a modified formulation, which demonstrated lower mean injection site pain versus the prior formulation. We are pleased to see the results support the use of ENBREL as a monotherapy agent in psoriatic arthritis and look forward to evaluating these data further."

In SEAM-PsA, patients were randomly assigned to one of the three treatment groups. At 24 weeks, patients were assessed for ACR 20 response, a standard measure of 20 percent or greater improvement from baseline in ACR response criteria, a composite measure based on tender and swollen joint counts, patient assessment of pain, patient and physician global assessment of disease activity, patient assessment of physical function and a measure of inflammation called the acute-phase reactant value. The patients were also assessed for MDA, a PsA-specific composite measure assessing disease activity based on a number of clinical domains, including inflammation of joints and entheses (where tendons and ligaments connect to bone), skin disease, patient-reported outcomes and functional disability.

The use of ENBREL monotherapy and combination therapy was also assessed across a number of other PsA outcomes, including x-ray endpoints. Skin assessments included the percent improvement in psoriasis-affected body surface area (BSA), and percent of patients who achieved clear or almost clear skin status, based on Static Physician Global Assessment of Psoriasis.

Adverse events, serious adverse events, and adverse events leading to discontinuation of the investigational products or study were generally balanced between the treatment groups. Adverse events occurring in 5 percent or more of patients receiving ENBREL included nausea, nasopharyngitis, upper respiratory tract infection, headache and bronchitis. Adverse events observed in patients treated with ENBREL were generally consistent with the known safety profile of ENBREL. No new safety concerns were identified in this study.

Additionally, a Phase 3b, multicenter, randomized, double-blind crossover study showed that a modified ENBREL formulation was associated with significantly lower mean injection site pain (ISP), compared with the prior formulation, in adult patients with either moderate-to-severe rheumatoid arthritis (RA) or PsA. The mean ISP visual analog scale (VAS) score was 23.1 mm for the prior formulation and 19.1 mm for the modified formulation for a mean difference in ISP between prior and modified formulations across all patients of 4.0 mm on a 100 mm scale [95 percent CI; 0.03, 7.98], *p*=0.048. Patients with higher ISP scores with the prior formulation showed greater reduction in ISP with the modified formulation. Patients with ISP scores above the mean with the prior formulation showed a mean difference of 12.2 mm [95 percent CI: 3.1, 21.3] with the new formulation and patients who were below the mean the results were similar between both groups (-0.9 mm [95 percent CI: –3.9, 2.1]). Adverse events were similar to

those seen in previous studies in adults with moderate-to-severe RA and PsA. This modified formulation was introduced in 2017 in conjunction with the ENBREL Mini® with AutoTouch® and is now also available across ENBREL delivery device options.

About SEAM-PsA
Study of **E**tanercept **A**nd **M**ethotrexate in subjects with **Ps**oriatic **A**rthritis (SEAM-PsA) is a Phase 3, multicenter, double-blind, randomized controlled study conducted in biologic-naïve patients, with no prior use of methotrexate for PsA. Patients were assigned 1:1:1 to one of the three treatment groups and followed for a total of 48 weeks. At 24 weeks, patients were assessed for ACR 20 response and MDA criteria, along with additional secondary and exploratory endpoints. Patients with inadequate response were provided rescue treatment of ENBREL plus methotrexate combination therapy for the remainder of the study, though remained blind.

About Psoriatic Arthritis
Psoriatic arthritis is a chronic, inflammatory form of arthritis which can cause swelling, stiffness and pain in and around the joints that worsens over time. It may also include red patches of skin topped with silvery scales, or skin lesions. If left untreated, PsA can have disabling results. Appropriate diagnosis and treatment can help manage symptoms and may help stop further irreversible joint damage.

About Enbrel® (etanercept)
ENBREL is a soluble form of a tumor necrosis factor (TNF) receptor with a clinical efficacy and safety profile established over 20 years of collective clinical experience. ENBREL was first approved in 1998 for moderate-to-severe rheumatoid arthritis. ENBREL was approved in 1999 to treat moderate-to-severe polyarticular juvenile idiopathic arthritis, in 2002 to treat psoriatic arthritis, in 2003 for the treatment of patients with ankylosing spondylitis, in 2004 to treat moderate-to-severe plaque psoriasis in adults, and in 2016 the moderate-to-severe plaque psoriasis indication was expanded to include patients 4 years or older. Prescription ENBREL is given by injection.

ENBREL indications in the U.S.:

- ENBREL is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately-to-severely active rheumatoid arthritis (RA). ENBREL can be initiated in combination with methotrexate (MTX) or used alone.
- ENBREL is indicated for reducing signs and symptoms of moderately-to-severely active polyarticular juvenile idiopathic arthritis in patients ages two and older.
- ENBREL is indicated for reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with psoriatic arthritis. ENBREL can be used with or without methotrexate.
- ENBREL is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.
- ENBREL is indicated for the treatment of patients 4 years or older with chronic moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

ENBREL U.S. Important Safety Information

Patients treated with ENBREL are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids or were predisposed to infection because of their underlying disease. ENBREL should not be initiated in the presence of sepsis, active infections, or allergy to ENBREL or its components. ENBREL should be discontinued if a patient develops a serious infection or sepsis. Reported infections include: 1) Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent TB before ENBREL use and periodically during therapy. Treatment for latent infection should be initiated prior to ENBREL use, 2) Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric antifungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness, and 3) Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.

The risks and benefits of treatment with ENBREL should be carefully considered prior to initiating therapy in patients 1) with chronic or recurrent infection, 2) who have been exposed to TB, 3) who have resided or traveled in areas of endemic TB or endemic mycoses, or 4) with underlying conditions that may predispose them to infections such as advanced or poorly controlled diabetes. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with ENBREL, including the possible development of TB in patients who tested negative for latent TB prior to initiating therapy.

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with tumor necrosis factor (TNF) blockers, including ENBREL.

In adult clinical trials of all TNF blockers, more cases of lymphoma were seen compared to control patients. The risk of lymphoma may be up to several-fold higher in RA patients. The role of TNF blocker therapy in the development of malignancies is unknown. Cases of acute and chronic leukemia have been reported in association with postmarketing TNF blocker use in RA and other indications. The risk of leukemia may be higher in patients with RA (approximately 2-fold) than the general population. Melanoma and non-melanoma skin cancer (NMSC) have been reported in patients treated with TNF blockers, including ENBREL. Periodic skin examinations should be considered for all patients at increased risk for skin cancer. In patients who initiated therapy at ≤ 18 years of age, approximately half of the reported malignancies were lymphomas (Hodgkin's and non-Hodgkin's lymphoma). Other cases included rare malignancies usually associated with immunosuppression and malignancies that are not usually observed in children and adolescents. Most of the patients were receiving concomitant immunosuppressants.

Treatment with TNF-blocking agents, including ENBREL, has been associated with rare (< 0.1%) cases of new onset or exacerbation of central nervous system demyelinating disorders, some presenting with mental status changes and some associated with permanent disability, and with peripheral nervous system demyelinating disorders. Cases of transverse myelitis, optic neuritis, multiple sclerosis, Guillain-Barré syndromes, other peripheral demyelinating neuropathies, and new onset or exacerbation of seizure disorders have been reported in postmarketing experience with

ENBREL therapy. Prescribers should exercise caution in considering the use of ENBREL in patients with preexisting or recent-onset central or peripheral nervous system demyelinating disorders.

Cases of worsening congestive heart failure (CHF) and, rarely, new-onset cases have been reported in patients taking ENBREL. Caution should be used when using ENBREL in patients with CHF. These patients should be carefully monitored. Rare cases of pancytopenia, including aplastic anemia, some fatal, have been reported. The causal relationship to ENBREL therapy remains unclear. Exercise caution when considering ENBREL in patients who have a previous history of significant hematologic abnormalities. Advise patients to seek immediate medical attention if they develop signs or symptoms of blood dyscrasias or infection. Consider discontinuing ENBREL if significant hematologic abnormalities are confirmed. Reactivation of hepatitis B has been reported in patients who were previously infected with hepatitis B virus (HBV) and received concomitant TNF-blocking agents, including ENBREL. Most reports occurred in patients also taking immunosuppressive agents, which may contribute to hepatitis B reactivation. Exercise caution when considering ENBREL in these patients.

Allergic reactions associated with administration of ENBREL during clinical trials have been reported in < 2% of patients. If an anaphylactic reaction or other serious allergic reaction occurs, administration of ENBREL should be discontinued immediately and appropriate therapy initiated. Live vaccines should not be administered to patients on ENBREL. Pediatric patients, if possible, should be brought up to date with all immunizations prior to initiating ENBREL. In patients with exposure to varicella virus, temporarily discontinue ENBREL and consider prophylactic treatment with Varicella Zoster Immune Globulin. Autoantibodies may develop with ENBREL, and rarely lupus-like syndrome or autoimmune hepatitis may occur. These may resolve upon withdrawal of ENBREL. Stop ENBREL if lupus-like syndrome or autoimmune hepatitis develops. The use of ENBREL in patients with Wegener's granulomatosis receiving immunosuppressive agents (e.g., cyclophosphamide) is not recommended. Based on a study of patients treated for alcoholic hepatitis, exercise caution when using ENBREL in patients with moderate-to-severe alcoholic hepatitis.

The most commonly reported adverse reactions in RA clinical trials were injection site reaction and infection. In clinical trials of all other adult indications, adverse reactions were similar to those reported in RA clinical trials. In general, the adverse reactions in pediatric patients were similar in frequency and type as those seen in adult patients. The types of infections reported in pediatric patients were generally mild and consistent with those commonly seen in the general pediatric population.

The use of ENBREL in patients receiving concurrent cyclophosphamide therapy is not recommended. The risk of serious infection may increase with concomitant use of abatacept therapy. Concurrent therapy with ENBREL and anakinra is not recommended. Hypoglycemia has been reported following initiation of ENBREL therapy in patients receiving medication for diabetes, necessitating a reduction in anti-diabetic medication in some of these patients.

Please see Prescribing Information and Medication Guide at www.ENBREL.com

About Amgen
Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be one of the world's leading independent biotechnology companies, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

Amgen Forward-Looking Statements
This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements 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 annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and current reports on Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

No forward-looking statement can be guaranteed and actual results may differ materially from those we project. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for us to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints we have selected. We develop product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as we may have believed at the time of entering into such relationship. Also, we or others could identify safety, side effects or manufacturing problems with our products, including our devices, after they are on the market.

Our results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing our products and global economic conditions. In addition, sales of our products are affected by pricing pressure, political and public scrutiny and reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Our business may be impacted by government investigations, litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax

liabilities. Further, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. The discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to acquire other companies or products and to integrate the operations of companies we have acquired may not be successful. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of our systems and our data. Our stock price is volatile and may be affected by a number of events. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

CONTACT: Amgen, Thousand Oaks
Kristen Davis, 805-447-3008 (media)
Kristen Neese, 805-313-8267 (media)
Arvind Sood, 805-447-1060 (investors)

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