Fremanezumabdata publicerad i *The Lancet* visar på kliniskt betydelsefull reduktion av antalet månatliga migrändagar jämfört med placebo för patienter med svårbehandlad migrän

FOCUS-studien utvärderade Fremanezumabs effekt och säkerhet som preventiv behandling av migrän hos vuxna patienter som tidigare behandlats, utan tillfredsställande resultat, med två till fyra olika klasser migränprofylaktika. Behandling med fremanezumab visade sig vara effektiv jämfört med placebo.

JERUSALEM, August 21, 2019 – Teva Pharmaceutical Industries Ltd. (NYSE och TASE: TEVA) meddelade idag att resultaten från fas IIIb FOCUS-studien publicerats online före publicering av den tryckta versionen av *The Lancet*. FOCUS-studien undersökte fremanezumab vs placebo hos vuxna migränpatienter som tidigare upplevt otillräcklig effekt av två till fyra klasser av förebyggande behandlingar. Studien fann att fremanezumab var överlägset placebo för alla primära och sekundära effektmått.

Det primära effektmåttet för studien var genomsnittlig förändring från baslinjen i det månatliga antalet migrändagar under en 12-veckors behandlingsperiod efter den första dosen. Behandlingen resulterade i statistiskt signifikanta minskningar av det genomsnittliga antalet månatliga migrändagar hos deltagare som under studien fick antingen kvartals- eller månadsdosering med fremanezumab.

“As a physician, it is extremely rewarding to see that patients with very difficult-to-treat migraine experienced clinically significant improvement with fremanezumab,” said Professor Michel D. Ferrari, MD, PhD, lead author and Chair Leiden Centre for Translational Neuroscience, Leiden University Medical Centre, Leiden, The Netherlands. “More than a third of patients achieved a clinically meaningful 50% reduction in monthly migraine days within just four weeks of initiating treatment.”

Fremanezumab is approved in the U.S. and Europe for the preventive treatment of migraine in adults. The FOCUS study, a randomized, double-blind, parallel-group, placebo controlled study, evaluated the efficacy of two dosing regimens of fremanezumab (675 mg quarterly or 225 mg monthly) in a large population of adult patients (aged 18-70) with episodic or chronic migraine who had documented prior inadequate response* within the past ten years to two-to-four pharmacological classes of migraine preventive medications: beta blockers, anticonvulsants, tricyclic antidepressants (amitriptyline), calcium channel blockers (flunarizine), angiotensin II receptor antagonists (candesartan), onabotulinumtoxinA, or valproic acid.

Between November 2017 and July 2018, 838 patients with episodic (39 percent) or chronic (61 percent) migraine were randomized (1:1:1) by electronic interactive response technology (IRT) at 104 sites in 14 countries to placebo (n=279), quarterly fremanezumab (n=276), or monthly fremanezumab (n=283). Both patients with and without overuse of acute headache medication were included. Reductions from baseline in monthly days with migraine, moderate to severe headache, or use of acute headache medications were about 3.5 days (30 percentage points) greater with fremanezumab than with placebo ($p<0.0001$). The odds relative to placebo for achieving a ≥50 percent reduction in migraine days as early as four weeks after starting study treatment were approximately six-fold higher with fremanezumab ($p<0.0001$). Patients treated with fremanezumab had 3.1- to 3.8-day greater reductions in migraine days (from 9.4 to 17.1 days at baseline) across dosing and migraine classification subgroups than patients receiving placebo ($p<0.0001$), representing a therapeutic gain of 26 to 39 percentage points.

“Migraine can be debilitating for patients – and frustrating for those who have failed multiple preventive treatments,” said Joshua M. Cohen, MD, MPH, FAHS, Global Medical Lead for Migraine & Headache at Teva. “We continue our clinical trial efforts in the area of migraine research and we are very pleased with the FOCUS results. Fremanezumab shows promise for patients with migraine, and being published in the *Lancet*, a very prestigious medical journal, demonstrates the value of the clinical work being done at Teva to support and elevate the need for migraine education and treatment.”

IR Contacts	**United States**	Kevin C. Mannix	(215) 591-8912
		Ran Meir	972 (3) 926-7516
PR Contacts	**United States**	Doris Saltkill	(913) 777-3343
	Israel	Yonatan Beker	972 (54) 888 5898

The most common adverse reactions in the study were injection site reactions. Less than 1 percent of patients in the fremanezumab group experienced an adverse event leading to discontinuation. Patients with major comorbid diseases, including major cardiovascular disease, were excluded from participation in this study.

**Inadequate response was defined as no clinically meaningful improvement after at least three months of therapy at a stable dose, per the treating physician's judgement; discontinuation due to adverse events that made treatment intolerable; or the treatment was contraindicated or unsuitable for the preventive treatment of migraine for the patient. Documentation of prior failure to migraine preventive medication was generally based on the patient's medical record, with the medication name, treatment duration, dose level and reason for discontinuation. If obtaining the medical record was not possible, the treating physician could provide an affidavit confirming prior treatment failures according to the protocol definition.*

About Fremanezumab

Fremanezumab is available as a 225 mg/1.5mL single dose injection in a prefilled syringe with two dosing options – 225 mg monthly administered as one subcutaneous injection, or 675 mg every three months (quarterly), administered as three subcutaneous injections. Fremanezumab can be administered in office by a healthcare professional or at home by a patient or caregiver. No starting dose is required to begin treatment. Fremanezumab is marketed in the United States as AJOVY® (fremanezumab-vfrm) injection and as AJOVY®▼ in Europe.

U. S. Important Safety Information about AJOVY
AJOVY is indicated for the preventive treatment of migraine in adults.

Contraindications: AJOVY is contraindicated in patients with serious hypersensitivity to fremanezumab-vfrm or to any of the excipients.

Hypersensitivity Reactions: Hypersensitivity reactions, including rash, pruritus, drug hypersensitivity, and urticaria were reported with AJOVY in clinical trials. Most reactions were mild to moderate, but some led to discontinuation or required corticosteroid treatment. Most reactions were reported from within hours to one month after administration. If a hypersensitivity reaction occurs, consider discontinuing AJOVY and institute appropriate therapy.

Adverse Reactions: The most common adverse reactions (≥5% and greater than placebo) were injection site reactions.

Please click here for full U. S. Prescribing Information for AJOVY® (fremanezumab-vfrm) injection.

Information for Europe about AJOVY▼ can be found here.
AJOVY is indicated to prevent migraine in adults who have at least four migraine days a month.

▼Adverse events should be reported.

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events.

Reporting forms and information can be found at https:// www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Teva – please refer to local numbers.

About Teva

Teva Pharmaceutical Industries Ltd. (NYSE and TASE: TEVA) has been developing and producing medicines to improve people's lives for more than a century. We are a global leader in generic and specialty medicines with a portfolio consisting of over 3,500 products in nearly every therapeutic area. Around 200 million people around the world take a Teva medicine every day, and are served by one of the largest and most complex supply chains in the

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pharmaceutical industry. Along with our established presence in generics, we have significant innovative research and operations supporting our growing portfolio of specialty and biopharmaceutical products. Learn more at www.tevapharm.com.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 regarding fremanezumab, which are based on management's current beliefs and expectations and are subject to substantial risks and uncertainties, both known and unknown, that could cause our future results, performance or achievements to differ significantly from that expressed or implied by such forward-looking statements. Important factors that could cause or contribute to such differences include risks relating to:

- challenges inherent in product research and development, including uncertainty of clinical success and obtaining regulatory approvals;
- our ability to successfully compete in the marketplace, including: that we are substantially dependent on our generic products; competition for our specialty products, especially COPAXONE®, our leading medicine, which faces competition from existing and potential additional generic versions and orally-administered alternatives; the uncertainty of commercial success of AJOVY® or AUSTEDO®; competition from companies with greater resources and capabilities; efforts of pharmaceutical companies to limit the use of generics, including through legislation and regulations; consolidation of our customer base and commercial alliances among our customers; the increase in the number of competitors targeting generic opportunities and seeking U.S. market exclusivity for generic versions of significant products; price erosion relating to our products, both from competing products and increased regulation; delays in launches of new products and our ability to achieve expected results from investments in our product pipeline; our ability to take advantage of high-value opportunities; the difficulty and expense of obtaining licenses to proprietary technologies; and the effectiveness of our patents and other measures to protect our intellectual property rights
- our substantial indebtedness, which may limit our ability to incur additional indebtedness, engage in additional transactions or make new investments, may result in a further downgrade of our credit ratings; and our inability to raise debt or borrow funds in amounts or on terms that are favorable to us;
- our business and operations in general, including: failure to effectively execute our restructuring plan announced in December 2017; uncertainties related to, and failure to achieve, the potential benefits and success of our senior management team and organizational structure; harm to our pipeline of future products due to the ongoing review of our R&D programs; our ability to develop and commercialize additional pharmaceutical products; potential additional adverse consequences following our resolution with the U.S. government of our FCPA investigation; compliance with sanctions and other trade control laws; manufacturing or quality control problems, which may damage our reputation for quality production and require costly remediation; interruptions in our supply chain; disruptions of our or third party information technology systems or breaches of our data security; the failure to recruit or retain key personnel; variations in intellectual property laws that may adversely affect our ability to manufacture our products; challenges associated with conducting business globally, including adverse effects of political or economic instability, major hostilities or terrorism; significant sales to a limited number of customers in our U.S. market; our ability to successfully bid for suitable acquisition targets or licensing opportunities, or to consummate and integrate acquisitions; implementation of a new enterprise resource planning system that, if deficient, could materially and adversely affect our operations and/or the effectiveness of our internal controls; and our prospects and opportunities for growth if we sell assets;
- compliance, regulatory and litigation matters, including: costs and delays resulting from the extensive governmental regulation to which we are subject; the effects of reforms in healthcare regulation and reductions in pharmaceutical pricing, reimbursement and coverage; increased legal and regulatory action in connection with public concern over the abuse of opioid medications in the U.S.; governmental investigations into selling and marketing practices; potential liability for patent infringement; product liability claims; increased government scrutiny of our patent settlement agreements; failure to comply with complex Medicare and Medicaid reporting and payment obligations; and environmental risks;

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- other financial and economic risks, including: our exposure to currency fluctuations and restrictions as well as credit risks; potential impairments of our intangible assets; potential significant increases in tax liabilities; and the effect on our overall effective tax rate of the termination or expiration of governmental programs or tax benefits, or of a change in our business;

and other factors discussed in our Quarterly Reports on Form 10-Q for the first and second quarter of 2019 and in our Annual Report on Form 10-K for the year ended December 31, 2018, including in the sections captioned "Risk Factors" and "Forward Looking Statements." Forward-looking statements speak only as of the date on which they are made, and we assume no obligation to update or revise any forward-looking statements or other information contained herein, whether as a result of new information, future events or otherwise. You are cautioned not to put undue reliance on these forward-looking statements.

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