Aytu BioPharma Highlights Opportunity for EXXUATM (gepirone) as New Way to Treat Major Depressive Disorder That Avoids Common Side Effects of Sexual Dysfunction and Significant Weight Gain following launch of EXXUA

EXXUA addresses frequent causes of treatment discontinuation with first-line SSRIs and SNRIs

Now commercially available through retail pharmacies and participating Aytu RxConnect® pharmacies to support patient access

DENVER, COLORADO / ACCESS Newswire / January 20, 2026 / Aytu BioPharma, Inc. (the "Company" or "Aytu") (Nasdaq:AYTU), a pharmaceutical company focused on advancing innovative medicines to treat complex central nervous system disorders and improve the quality of life of patients, today announced the nationwide commercial launch of EXXUA and successful completion of its launch meeting last week that finalized sales training and launch preparations for EXXUA, the first and only selective 5-HT1A agonist approved by the United States Food and Drug Administration for the treatment of major depressive disorder ("MDD") in adults, representing a new way to treat MDD.

EXXUA is a once-daily monotherapy with a unique mechanism of action that selectively targets 5-HT1A receptors, important regulators of mood and emotion,[1-3] while minimizing activity at serotonin receptors (eg, 5-HT2A) linked to side effects such as sexual dysfunction[4] and weight gain[5,6] that are common with many first-line antidepressants. EXXUA is only approved for use in adults. Antidepressants increase the risk of suicidal thoughts and behaviors in pediatric and young adult patients in short-term studies.

Of the 21 million Americans living with MDD, up to 70%[2,7] experience treatment-emergent sexual dysfunction and more than 65%[8] are affected by weight gain, two side effects of first-line MDD medications that drive nearly half of patients to discontinue their treatment.[9]

"The burden of MDD is not limited to psychological symptoms," said Dr. Stephen Stahl, Professor of Psychiatry, University of California and founder of the Neuroscience Education Institute, a recognized expert neuropsychopharmacologist. "Sexual dysfunction and weight gain are frequently experienced as core features of depression, reflecting the disorder's broad impact on both emotional and physical health. Left unaddressed, these symptoms can then intensify the depressive experience and perpetuate its impact. The tragedy for many patients is that today's treatments-while effective for depression-often exacerbate these very physical symptoms, asking patients to trade one burden for another. The ability to manage

depression effectively without disrupting the intimacy and connection patients value is tremendous in terms of quality of life."

"Completing our EXXUA launch meeting marks a significant milestone for Aytu as we transition from preparation to execution," said Josh Disbrow, CEO of Aytu BioPharma. "Our team is well-equipped to have informed, meaningful conversations with clinicians about EXXUA, supported by strong clinical evidence and a clear understanding of MDD patients' needs."

To learn more about the science behind EXXUA and how it was studied, please visit EXXUA.com.

About Aytu BioPharma

Aytu is a specialty pharmaceutical company focused on advancing innovative medicines for complex central nervous system disorders to improve the quality of life for patients. The Company's prescription products include EXXUA™ (gepirone) extended-release tablets (see Full Prescribing Information, including Boxed Warning) for the treatment of major depressive disorder (MDD), and treatments for attention-deficit/hyperactivity disorder (ADHD). Aytu is committed to delivering the Company's medications through best-in-class patient access programs that help to enable optimal patient outcomes. For more information, please visit aytubio.com or follow us on LinkedIn.

About EXXUA

EXXUA is a novel oral selective serotonin 5-HT1A receptor agonist indicated for the treatment of major depressive disorder (MDD) in adults.

IMPORTANT SAFETY INFORMATION

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

Antidepressants increase the risk of suicidal thoughts and behaviors in pediatric and young adult patients in short-term studies. Closely monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors. EXXUA is not approved for use in pediatric patients.

INDICATIONS AND USAGE

EXXUA is indicated for the treatment of major depressive disorder (MDD) in adults.

DOSAGE AND ADMINISTRATION

Important Recommendations Prior to Initiating and During Treatment with EXXUA

Electrocardiogram and Electrolyte Monitoring

Correct electrolyte abnormalities prior to initiating EXXUA. In patients with electrolyte abnormalities, or who are receiving diuretics or glucocorticoids, or who have a history of hypokalemia or hypomagnesemia, also monitor electrolytes during dose titration and periodically during treatment with EXXUA.

Perform an electrocardiogram (ECG) prior to initiating EXXUA, during dosage titration, and periodically during treatment. Do not initiate EXXUA if QTc is > 450 msec at baseline. Monitor ECGs more frequently if EXXUA is used:

- concomitantly with drugs known to prolong the QT interval
- in patients who develop QTc 450 msec during treatment
- in patients with a significant risk of developing torsade de pointes

Do not escalate the EXXUA dosage if the QTcF is > 450 msec.

Bipolar Disorder, Mania, and Hypomania Screening

Screen patients for a personal or family history of bipolar disorder, mania, or hypomania prior to initiating treatment with EXXUA.

Important Administration Instructions

Take EXXUA orally with food at approximately the same time each day. Swallow tablets whole. Do not split, crush, or chew EXXUA.

Recommended Dosage

The recommended starting dosage of EXXUA is 18.2 mg once daily. Based on clinical response and tolerability, the dosage may be increased to 36.3 mg orally once daily on Day 4 and further titrated to 54.5 mg orally once daily after Day 7 and to 72.6 mg orally once daily after an additional week. The maximum recommended daily dosage of EXXUA is 72.6 mg once daily.

Dosage Recommendations in Geriatric Patients

The recommended starting dosage of EXXUA in geriatric patients is 18.2 mg orally once daily. Based on clinical response and tolerability, the dosage may be increased to maximum recommended dosage of 36.3 mg orally once daily after Day 7.

Recommended Dosage in Patients with Renal Impairment

The recommended starting dosage of EXXUA in patients with creatinine clearance < 50 mL/min is 18.2 mg orally once daily. Based on clinical response and tolerability, the dosage

may be increased to the maximum recommended dosage of 36.3 mg orally once daily after Day 7. The recommended dosage in patients with creatinine clearance 50 mL/min is the same as in patients with normal renal function.

Recommended Dosage in Patients with Hepatic Impairment

The recommended starting dose of EXXUA in patients with moderate (Child-Pugh B) hepatic impairment is 18.2 mg once daily. Based on clinical response and tolerability, the dosage may be increased to the maximum recommended dosage of 36.3 mg orally once daily after Day 7. EXXUA is contraindicated in patients with severe (Child-Pugh C) hepatic impairment. The recommended dosage in patients with mild (Child-Pugh A) hepatic impairment is the same as patients with normal hepatic function.

Dosage Modifications for Concomitant Use with CYP3A4 Inhibitors

Reduce the EXXUA dose by 50% when used concomitantly with a moderate CYP3A4 inhibitor. EXXUA is contraindicated in patients receiving strong CYP3A4 inhibitors.

Switching a Patient to or from a Monoamine Oxidase Inhibitor (MAOI) Antidepressant

At least 14 days must elapse between discontinuation of an MAOI intended to treat depression and initiation of therapy with EXXUA. Conversely, at least 14 days must be allowed after stopping EXXUA before starting an MAOI antidepressant.

CONTRAINDICATIONS

EXXUA is contraindicated in patients:

- with known hypersensitivity to gepirone or components of EXXUA.
- with prolonged QTc interval > 450 msec at baseline.
- with congenital long QT syndrome.
- receiving concomitant strong CYP3A4 inhibitors.
- with severe hepatic impairment.
- taking, or within 14 days of stopping, MAOIs due to the risk of serious and possibly fatal drug interactions, including hypertensive crisis and serotonin syndrome. Starting EXXUA in a patient treated with reversible MAOIs such as linezolid or intravenous methylene blue is also contraindicated.

WARNINGS AND PRECAUTIONS

Suicidal Thoughts and Behaviors in Adolescents and Young Adults

In pooled analyses of placebo-controlled trials of antidepressant drugs (SSRIs and other antidepressant classes) that included approximately 77,000 adult patients, and 4,500

pediatric patients, the incidence of suicidal thoughts and behaviors in antidepressant-treated patients aged 24 years and younger was greater than in placebo-treated patients.

There was considerable variation in risk of suicidal thoughts and behaviors among drugs, but there was an increased risk identified in young patients for most drugs studied. There were differences in absolute risk of suicidal thoughts and behaviors across the different indications, with the highest incidence in patients with MDD.

***EXXUA is not approved for use in pediatric patients.**

Monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy, and at times of dosage changes. Counsel family members or caregivers of patients to monitor for changes in behavior and to alert the healthcare provider. Consider changing the therapeutic regimen, including possibly discontinuing EXXUA, in patients whose depression is persistently worse, or who are experiencing emergent suicidal thoughts or behaviors.

QT Prolongation

EXXUA prolongs the QTc interval.

- EXXUA is contraindicated in patients with congenital long QT syndrome and in patients with severe hepatic impairment or in patients receiving concomitant strong CYP3A4 inhibitors as they increase EXXUA plasma concentrations.
- Do not initiate EXXUA if QTc is > 450 msec at baseline.
- Correct electrolyte abnormalities prior to EXXUA initiation. In patients with electrolyte abnormalities, who are receiving diuretics or glucocorticoids, or have a history or hypokalemia or hypomagnesemia, also monitor electrolytes during dose titration and periodically during treatment with EXXUA.
- Perform an ECG prior to EXXUA initiation, during dosage titration, and periodically during treatment. Monitor patients with ECGs more frequently:
    - If EXXUA is used concomitantly with drugs known to prolong the QT interval.
    - In patients who develop QTc 450 msec during treatment with EXXUA. Do not escalate the EXXUA dosage if QTcF is > 450 msec.
    - In patients with a significant risk of developing torsade de pointes, including those with uncontrolled or significant cardiac disease, recent myocardial infarction, heart failure, unstable angina, bradyarrhythmias, uncontrolled hypertension, high degree atrioventricular block, severe aortic stenosis, or uncontrolled hypothyroidism.
- Reduce the EXXUA dosage when used concomitantly with moderate CYP3A4 inhibitors, as they may increase EXXUA concentrations.

Serotonin Syndrome

Concomitant use of EXXUA with SSRIs or tricyclic antidepressants may cause serotonin syndrome, a potentially life-threatening condition with changes including altered mental

status, hypertension, restlessness, myoclonus, hyperthermia, hyperreflexia, diaphoresis, shivering, and tremor. The concomitant use of EXXUA with MAOIs is contraindicated. In addition, do not initiate EXXUA in a patient being treated with MAOIs such as linezolid or intravenous methylene blue. If it is necessary to initiate treatment with an MAOI such as linezolid or intravenous methylene blue in a patient taking EXXUA discontinue EXXUA before initiating treatment with the MAOI.

If concomitant use of EXXUA with other serotonergic drugs is clinically warranted, inform patients of the increased risk for serotonin syndrome and monitor for symptoms. Discontinue EXXUA and/or concomitant serotonergic drug immediately if the above symptoms occur and initiate supportive symptomatic treatment.

Activation of Mania or Hypomania

Antidepressant treatment can precipitate a manic, mixed, or hypomanic manic episode. The risk appears to be increased in patients with bipolar disorder or who have risk factors for bipolar disorder. Prior to initiating treatment with EXXUA, screen patients for a history of bipolar disorder and the presence of risk factors for bipolar disorder (e.g., family history of bipolar disorder, suicide, or depression). EXXUA is not approved for use in treating bipolar depression.

ADVERSE REACTIONS

Most common adverse reactions (incidence of 5% and at least twice incidence of placebo) were dizziness, nausea, insomnia, abdominal pain, and dyspepsia.

The following adverse reactions are discussed in greater detail in other sections of the labeling:

- Suicidal Thoughts and Behaviors in Adolescents and Young Adults
- QT Prolongation
- Serotonin Syndrome
- Activation of Mania or Hypomania

To report SUSPECTED ADVERSE REACTIONS, contact Aytu BioPharma at 1-855-298-8246 or http://www.exxua.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Pregnancy

The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth

defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to antidepressants, including EXXUA, during pregnancy. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Antidepressants at 1-866-961-2388 or visiting online at https://womensmentalhealth.org/research/pregnancyregistry/antidepressants/.

Lactation

There is no data on the presence of gepirone in human milk, the effects on the breastfed infant, or the effects on milk production. Gepirone is present in rat milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk. There are reports of breastfed infants exposed to other serotonergic antidepressants experiencing irritability, restlessness, excessive somnolence, decreased feeding, and weight loss. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for EXXUA and any adverse effects on the breastfed infant from EXXUA or from the underlying maternal condition.

OVERDOSAGE

In clinical studies, cases of acute ingestions up to 454 mg (6.25 times the maximum recommended dose) of EXXUA alone or in combination with other drugs, were reported. Signs and symptoms reported with overdose of EXXUA at doses up to 454 mg included vomiting and transient incomplete bundle branch block; an unknown dose of EXXUA produced altered level of consciousness and a 60-second convulsion. **No specific antidotes for EXXUA are known. Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.**

Please see Full Prescribing Information for EXXUA.

Forward-Looking Statements

This press release includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended ("Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended ("Exchange Act"). All statements other than statements of historical facts contained in this press release, are forward-looking statements. Forward-looking statements are generally written in the future tense and/or are preceded by words such as "may," "will," "should," "forecast," "could," "expect," "suggest," "believe," "estimate," "continue," "anticipate," "intend," "plan," or similar words, or the negatives of such terms or other variations on such terms or comparable terminology. All statements, other than statements of historical facts contained in this press release, are forward-looking

statements. These statements are predictions and are subject to risks and uncertainties that could cause the actual events or results to differ materially. These risks are described in “Risk Factors” in Part I, Item 1A of the Company’s most recent Annual Report on Form 10 K and in the other reports and documents it files with the United States Securities and Exchange Commission.

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