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AbbVie Announces Positive Topline Results from Phase 3 Trial of VENCLEXTA® (venetoclax) in Combination with Azacitidine in Patients with Acute Myeloid Leukemia (AML)

- VIALE-A study demonstrated statistically significant improvement in the primary endpoints of overall survival (OS) and composite complete remission rate (CR + CRi)
- AML is one of the most aggressive and difficult-to-treat blood cancers with a very low survival rate and few treatment options [1],[2]
- Full results will be presented at a future medical meeting or published in a peer-reviewed journal

NORTH CHICAGO, Ill., March 23, 2020 /PRNewswire/ -- AbbVie (NYSE: ABBV), a research-based global biopharmaceutical company, today announced the VIALE-A (M15-656) trial of VENCLEXTA® (venetoclax) in combination with azacitidine versus azacitidine in combination with placebo met its dual primary endpoints of statistically significant improvement of overall survival (OS) and composite complete remission rate (CR + CRi) for patients with previously-untreated acute myeloid leukemia (AML) who are ineligible for intensive chemotherapy. At the recommendation of an independent data monitoring committee (IDMC), and per the prespecified interim analysis plan, due to positive efficacy results at the first interim analysis for overall survival, the trial results will be reported early, and the data from the trial will be submitted to the U.S. FDA and global health authorities. Results will be presented at a future medical meeting or published in a peer-reviewed journal.

"For the past three decades, there has been few options for patients with AML who cannot receive or tolerate intensive chemotherapy or a bone marrow transplant," said Neil Gallagher, M.D., Ph.D., chief medical officer and vice president of development, AbbVie. "The positive results from VIALE-A support the clinical benefit of the venetoclax plus azacitidine combination in patients with AML who are ineligible for intensive chemotherapy and reflect our ongoing commitment to transform the standards of care for patients with hematologic malignancies."

AML is one of the most aggressive and difficult-to-treat blood cancers with a very low survival rate.[1,2] Despite advances in available therapies and care, the 5-year survival rate for patients diagnosed with AML remains approximately 28%.[3] AML typically worsens quickly, and due to age and comorbidities, not all patients are eligible to receive intensive chemotherapy.[4] AML is the most common acute leukemia in the world.[5] An estimated 160,000 people are currently living with the disease globally with an incidence rate of 103 new cases per 100,000 people.[5]

The Phase 3 VIALE-A study evaluated the efficacy and safety of venetoclax in combination with azacitidine compared with placebo in combination with azacitidine. The study met its dual primary endpoints of OS and composite complete remission (CR + CRi). At the recommendation of an IDMC, and per the prespecified interim analysis plan, due to positive efficacy results at the first interim analysis for overall survival, the trial results will be reported early, and the data from the trial will be submitted to the U.S. FDA and global health authorities. The observed safety profile is generally consistent with the known safety profile of venetoclax combined with azacitidine as observed in previous Phase 1/2 studies and the known safety profiles of the two medications.

In November 2018, AbbVie received accelerated approval in the U.S. for VENCLEXTA in combination with azacitidine, decitabine, or low-dose cytarabine (LDAC) for the treatment of newly-diagnosed AML in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy based on the Phase 1/2 studies. Approval was also granted in Mexico, Israel, Puerto Rico, Peru, Brazil, Russia, Argentina, Guatemala, Uruguay, Lebanon, Bahrain, Kazakhstan, Panama, Saudi Arabia, Taiwan, Australia, Qatar, and United Arab Emirates.

The Phase 3 VIALE-A and VIALE-C (M16-043) studies were conducted as confirmatory trials following the accelerated U.S. FDA approval of venetoclax in AML in 2018. In February 2020, AbbVie provided an update on the Phase 3 VIALE-C study of venetoclax in combination with LDAC compared with LDAC in combination with placebo.

VENCLEXTA is being developed by AbbVie and Roche. It is jointly commercialized by AbbVie and Genentech, a member of the Roche Group, in the U.S. and by AbbVie outside of the U.S.

About the VIALE-A (M15-656) Phase 3 Trial
A total of 443 treatment-naïve AML patients were enrolled and 433 were randomized in the double-blind, placebo-controlled Phase 3 VIALE-A trial. The trial was designed to evaluate the efficacy and safety of venetoclax in combination with azacitidine (n=287) compared with placebo in combination with azacitidine (n=146).[6]

About VENCLEXTA® (venetoclax)
VENCLEXTA® (venetoclax) is a first-in-class medicine that selectively binds and inhibits the B-cell lymphoma-2 (BCL-2) protein. In some blood cancers, BCL-2 prevents cancer cells from undergoing their natural death or self-destruction process, called apoptosis. VENCLEXTA targets the BCL-2 protein and works to help restore the process of apoptosis.

VENCLEXTA is being developed by AbbVie and Roche. It is jointly commercialized by AbbVie and Genentech, a member of the Roche Group, in the U.S. and by AbbVie outside of the U.S. Together, the companies are committed to BCL-2 research and to studying venetoclax in clinical trials across several blood and other cancers. VENCLEXTA is approved in more than 50 countries, including the U.S.

Uses and Important VENCLEXTA® (venetoclax) U.S. Safety Information[7]

Uses
VENCLEXTA is a prescription medicine used:

- to treat adults with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
- in combination with azacitidine, or decitabine, or low-dose cytarabine to treat adults with newly-diagnosed acute myeloid leukemia (AML) who:
  - are 75 years of age or older, **or**
  - have other medical conditions that prevent the use of standard chemotherapy.

VENCLEXTA was approved based on response rates. Continued approval for this use may depend on the results of an ongoing study to find out how VENCLEXTA works over a longer period of time.

It is not known if VENCLEXTA is safe and effective in children.

Important Safety Information

What is the most important information I should know about VENCLEXTA?

VENCLEXTA can cause serious side effects, including:

Tumor lysis syndrome (TLS). TLS is caused by the fast breakdown of cancer cells. TLS can cause kidney failure, the need for dialysis treatment, and may lead to death. Your healthcare provider will do tests to check your risk of getting TLS before you start taking VENCLEXTA. You will receive other medicines before starting and during treatment with VENCLEXTA to help reduce your risk of TLS. You may also need to receive intravenous (IV) fluids into your vein. Your healthcare provider will do blood tests to check for TLS when you first start treatment and during treatment with VENCLEXTA.

It is important to keep your appointments for blood tests. Tell your healthcare provider right away if you have any symptoms of TLS during treatment with VENCLEXTA, including fever, chills, nausea, vomiting, confusion, shortness of breath, seizures, irregular heartbeat, dark or cloudy urine, unusual tiredness, or muscle or joint pain.

Drink plenty of water when taking VENCLEXTA to help reduce your risk of getting TLS. Drink 6 to 8 glasses (about 56 ounces total) of water each day, starting 2 days before your first dose, on the day of your first dose of VENCLEXTA, and each time your dose is increased.

Your healthcare provider may delay, decrease your dose, or stop treatment with VENCLEXTA if you have side effects.

Who should not take VENCLEXTA?

Certain medicines must not be taken when you first start taking VENCLEXTA and while your dose is being slowly increased because of the risk of increased TLS.

- **Tell your health care provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. VENCLEXTA and other medicines may affect each other, causing serious side effects.
- Do not start new medicines during treatment with VENCLEXTA without first talking with your health care provider.

Before taking VENCLEXTA, tell your healthcare provider about all of your medical conditions, including if you:

- have kidney problems.
- have problems with your body salts or electrolytes, such as potassium, phosphorus, or calcium.
- have a history of high uric acid levels in your blood or gout.
- are scheduled to receive a vaccine. You should not receive a "live vaccine" before, during, or after treatment with VENCLEXTA, until your healthcare provider tells you it is okay. If you are not sure about the type of immunization or vaccine, ask your healthcare provider. These vaccines may not be safe or may not work as well during treatment with VENCLEXTA.
- are pregnant or plan to become pregnant. VENCLEXTA may harm your unborn baby. If you are able to become pregnant, your healthcare provider should do a pregnancy test before you start treatment with VENCLEXTA, and you should use effective birth control during treatment and for 30 days after the last dose of VENCLEXTA. If you become pregnant or think you are pregnant, tell your healthcare provider right away.
- are breastfeeding or plan to breastfeed. It is not known if VENCLEXTA passes into your breast milk. Do not breastfeed during treatment with VENCLEXTA.

What should I avoid while taking VENCLEXTA?
You should not drink grapefruit juice, or eat grapefruit, Seville oranges (often used in marmalades), or starfruit while you are taking VENCLEXTA. These products may increase the amount of VENCLEXTA in your blood.

What are the possible side effects of VENCLEXTA?

VENCLEXTA can cause serious side effects, including:

- **Low white blood cell counts (neutropenia).** Low white blood cell counts are common with VENCLEXTA, but can also be severe. Your healthcare provider will do blood tests to check your blood counts during treatment with VENCLEXTA.
- **Infections**. Death and serious infections such as pneumonia and blood infection (sepsis) have happened during treatment with VENCLEXTA. Your healthcare provider will closely monitor and treat you right away if you have a fever or any signs of infection during treatment with VENCLEXTA.

Tell your healthcare provider right away if you have a fever or any signs of an infection during treatment with VENCLEXTA.

The most common side effects of VENCLEXTA when used in combination with obinutuzumab or rituximab or alone in people with CLL or SLL include low white blood cell counts; low platelet counts; low red blood cell counts; diarrhea; nausea; upper respiratory tract infection; cough; muscle and joint pain; tiredness; and swelling of your arms, legs, hands, and feet.

The most common side effects of VENCLEXTA in combination with azacitidine, or decitabine, or low-dose cytarabine in people with AML include low white blood cell counts; nausea; diarrhea; low platelet counts; constipation; fever with low white blood cell counts; low red blood cell counts, infection in blood; rash; dizziness; low blood pressure; fever; swelling of your arms, legs, hands, and feet; vomiting; tiredness; shortness of breath; bleeding; infection in lung; stomach (abdominal) pain; pain in muscles or back; cough; and sore throat.

VENCLEXTA may cause fertility problems in males. This may affect your ability to father a child. Talk to your healthcare provider if you have concerns about fertility.

These are not all the possible side effects of VENCLEXTA. For more information, ask your healthcare provider or pharmacist.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit http://www.fda.gov/medwatch or call 1-800-FDA-1088.

If you cannot afford your medication, contact www.medicineassistancetool.org for assistance.

The full U.S. prescribing information, including Medication Guide, for VENCLEXTA can be found here.

Globally, prescribing information varies; refer to the individual country product label for complete information.

About AbbVie in Oncology
At AbbVie, we strive to discover and develop medicines that deliver transformational improvements in cancer treatment by uniquely combining our deep knowledge in core areas of biology with cutting-edge technologies, and by working together with our partners – scientists, clinical experts, industry peers, advocates, and patients. We remain focused on delivering these transformative advances in treatment across some of the most debilitating and widespread cancers. We are also committed to exploring solutions to help patients obtain access to our cancer medicines. AbbVie's oncology portfolio now consists of marketed medicines and a pipeline containing multiple new molecules being evaluated worldwide in more than 300 clinical trials and more than 20 different tumor types. For more information, please visit http://www.abbvie.com/oncology.

About AbbVie
AbbVie is a global, research and development-based biopharmaceutical company committed to developing innovative advanced therapies for some of the world's most complex and critical conditions. The company's mission is to use its expertise, dedicated people and unique approach to innovation to markedly improve treatments across four primary therapeutic areas: immunology, oncology, virology and neuroscience. In more than 75 countries, AbbVie employees are working every day to advance health solutions for people around the world. For more information about AbbVie, please visit us at www.abbvie.com. Follow @abbvie on Twitter, Facebook, LinkedIn or Instagram.

Forward-Looking Statements
Some statements in this news release are, or may be considered, forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995. The words "believe," "expect," "anticipate," "project" and similar expressions, among others, generally identify forward-looking statements. AbbVie cautions that these forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those indicated in the forward-looking statements. Such risks and uncertainties include, but are not limited to, competition from other products, challenges to intellectual property, difficulties inherent in the research and development process, adverse litigation or government action, and changes to laws and regulations applicable to our industry. Additional information about the economic, competitive, governmental, technological and other factors that may affect AbbVie's operations is set forth in Item 1A, "Risk Factors," of AbbVie's 2018 Annual Report on Form 10-K, which has been filed with the Securities and Exchange Commission. AbbVie undertakes no obligation to release publicly any revisions to forward-looking statements as a result of subsequent events or developments, except as required by law.

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[4] Pettit, K and Odenike, O. Defining and Treating Older Adults with Acute Myeloid Leukemia Who Are Ineligible for Intensive Therapies. Front Oncol. 2015; 5:250.

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[6] ClinicalTrials.gov (2019). NCT02993523: A Study of Venetoclax in Combination With Azacitidine Versus Azacitidine in Treatment Naïve Subjects With Acute Myeloid Leukemia Who Are Ineligible for Standard Induction Therapy. https://clinicaltrials.gov/ct2/show/NCT02993523.

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