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News Release

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New Data Demonstrate Long-Term Benefit of IMBRUVICA® (ibrutinib) as First-Line Treatment for High-Risk Chronic Lymphocytic Leukaemia

IMBRUVICA® (ibrutinib) pooled clinical trial analyses presented at ASH 2020 demonstrate sustained efficacy and safety in patients with historically poor outcomes

Data from real world evidence studies featured as oral presentations highlight the benefit of ibrutinib-based therapies in the first-line setting

BEERSE, BELGIUM, 06 December 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today results from pooled analyses of long-term follow-up from multiple clinical trials evaluating the use of IMBRUVICA® (ibrutinib) monotherapy and in combination as first-line treatment for patients with chronic lymphocytic leukaemia (CLL) with high-risk features. The data were presented at the 2020 American Society of Hematology (ASH) Annual Meeting. Results from an integrated analysis of two clinical trials with up to 79 months of follow-up (Abstract #2220)[1] demonstrated similar progression-free survival (PFS) and overall response rates (ORR) with ibrutinib in patients with or without high-risk genomic features, and further showed significant PFS

and ORR benefits with ibrutinib compared with chlorambucil-based therapy regardless of genomic risk features.[1]

In addition, data with a median follow-up of more than four years were presented from a pooled analysis of 89 patients with high-risk CLL bearing TP53 aberrations from four clinical trials showing that first-line treatment with ibrutinib resulted in sustained efficacy, including PFS, suggesting that ibrutinib has meaningfully improved the poor prognosis in this high-risk population (Abstract #2219).[2]

"These large integrated data sets with follow-up up to six years, in addition to other data presented at the meeting in similar populations, contribute to the accumulating evidence supporting the clinically meaningful, long-term treatment benefit of ibrutinib as first-line therapy for patients with CLL," said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC. "Ibrutinib is an approved standard of care in first-line treatment of CLL, and the data presented at the ASH Annual Meeting further demonstrate the durability of responses in CLL patients with traditional high-risk features."

Two additional studies will be presented in the oral sessions showing real-world treatment patterns or outcomes in patients with CLL treated outside of a clinical trial setting. The first study is a U.S. retrospective analysis describing treatment patterns and time to next treatment (TTNT) in patients with high-risk CLL treated with first-line ibrutinib or chemoimmunotherapy (CIT) (Abstract #372).[3] In this study, the largest of its kind to date, patients with high-risk CLL treated with single-agent ibrutinib had significantly longer TTNT compared with patients treated with first-line CIT.[3] In the second oral presentation, results from the U.S. informCLL™ registry (Abstract #547) highlighted infrequent prognostic biomarker testing rates prior to initiating CLL therapy, and limited use of such information to guide optimal treatment selection for many patients with high-risk CLL, suggesting an opportunity for additional education of healthcare providers.[4]

Integrated Analysis of the Phase 3 RESONATE-2 and iLLUMINATE Trials Evaluated Outcomes of First-Line Ibrutinib in Patients with CLL and High-Risk Genomic Features with up to 6.5 Years Follow-up (Abstract #2220)[1]

Data were presented from a pooled analysis of two Phase 3 studies (RESONATE-2 and iLLUMINATE) with up to 79 months of follow-up evaluating ibrutinib-based therapy in first-line treatment of CLL patients with various high-risk genomic features.[1]

Key Study Findings:

- In patients treated with ibrutinib-based therapy, PFS was comparable between patients with, versus without, specified high-risk genomic features, including del(17p)/TP53 mutated/BIRC3 mutated, the highest risk category.[1]
- At 42 months, PFS rates were significantly higher across all high-risk genomic subgroups in previously untreated patients treated with ibrutinib-based treatment (63 to 82 percent) compared with those receiving chlorambucil-based treatment (6 to 34 percent) with or without obinutuzumab, regardless of mutation.[1]
- At a median duration of ibrutinib treatment of 35.7-43.8 months across high-risk subgroups, there were no meaningful differences in the rates of treatment-emergent adverse events (AEs) of any Grade, or Grade 3 or greater AEs compared to those of the overall population.[1]

"Certain genomic abnormalities and mutations are predictors of inferior outcomes with chemoimmunotherapy in patients with CLL," said Jan A. Burger,* M.D., Ph.D., Professor, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, and principal study investigator. "Chemoimmunotherapy remains common in real-world practice despite evidence that shows small molecule inhibitor therapies like ibrutinib have demonstrated improved outcomes in high-risk patients compared to chemoimmunotherapy."

"Since its first European approval in 2014, ibrutinib has redefined treatment paradigms for CLL, and these study results offer further evidence of the benefits and tolerability ibrutinib offers to CLL patients," adds Dr Catherine Taylor, Vice

President, Medical Affairs Therapeutic Area Strategy, Europe, Middle East and Africa (EMEA), Janssen-Cilag Ltd., Middle East. "For high-risk CLL patients, the treatment landscape has advanced dramatically, with ibrutinib continuing to play a major role in defining what it means to live with genetic variations of this disease, which have historically poor outcomes."

Large, Pooled, Multi-Study Dataset Assessed Long-Term Benefit of First-Line Ibrutinib-Based Treatment in Patients with TP53 Aberrations with up to Four Years Follow-up (Abstract #2219)[2]

Data were presented from a pooled analysis of four clinical studies evaluating the long-term efficacy and safety of first-line ibrutinib-based therapy in CLL patients with TP53 aberrations present.[2] The four studies were: RESONATE2; iLLUMINATE; the E1912 study designed and conducted by the ECOG-ACRIN Cancer Research Group (ECOG-ACRIN) and sponsored by the National Cancer Institute (NCI), part of the National Institutes of Health (NIH); and the 1122e study sponsored by the National Heart, Lung, and Blood Institute (NHLBI).[2]

Key Study Findings:

- With a median follow-up of 50 months, median PFS was not reached (95% CI: 67 months to not estimable).[2] At 48 months, the PFS rate was 79 percent and the OS rate was 88 percent among high-risk patients treated with ibrutinib monotherapy.[2]
- Additionally, 46 percent of patients with TP53 aberrations remained on ibrutinib treatment and 39 percent had a complete response.[2]
- No new safety signals were identified in this analysis and in general the rates of Grade ≥3 AEs of clinical interest declined after the first year of ibrutinib treatment.[2]

Clinical Outcomes Among Real-World Patients with CLL Initiating First-Line Ibrutinib or Chemoimmunotherapy Stratified by Risk Status: Results From a U.S. Retrospective Chart Review Study (Abstract #372)[3]

Data were presented as an oral presentation from a large real-world study comparing clinical outcomes (TTNT) in high-risk and non-high-risk patients with CLL receiving ibrutinib compared to CIT in the first-line setting.[3]

Key Study Findings:

- Data presented showed that high-risk patients receiving ibrutinib significantly prolonged TTNT compared to those receiving CIT.[3]
- Ibrutinib also provided sustained clinical benefit regardless of risk status, which is consistent with clinical trial results.[5,6,7]
- This study highlighted the need for cytogenetic/molecular testing before CIT treatment, consistent with clinical treatment guidelines.[8,9]

Real-World Prognostic Biomarker Testing, Treatment Patterns, And Dosing Among Patients With CLL From the informCLL™ Prospective Observational Registry (Abstract #547)

An oral presentation on Monday, December 7, will feature results from the informCLL™ real-world prospective observational registry assessing treatment patterns in the era of novel agents.[4]

Key Study Findings:

- The most common index treatment was ibrutinib; the majority of patients treated with ibrutinib remained on therapy at two-year follow-up; and CIT was also used for one-third of patients.[4]
- Data also demonstrated that prognostic biomarker testing rates were poor, especially for the biomarkers TP53 and IGHV.[4]
- Data from informCLL™ also indicate a 'knowledge gap' in terms of prognostic marker testing, interpretation and selection of optimal therapies for patients with high-risk disease.[4]

**Jan A. Burger is a principal study investigator and was not compensated for any media work*

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About Ibrutinib

Ibrutinib is a once-daily, first-in-class Bruton's tyrosine kinase (BTK) inhibitor that is administered orally, and is jointly developed and commercialised by Janssen Biotech, Inc. and Pharmacyclics LLC, an AbbVie company.[10] Ibrutinib blocks the BTK protein; the BTK protein sends important signals that tell B cells to mature and produce antibodies. BTK signalling is needed by specific cancer

cells to multiply and spread.[11] By blocking BTK, ibrutinib may help move abnormal B cells out of their nourishing environments in the lymph nodes, bone marrow, and other organs.[12]

Indications for which ibrutinib is approved in Europe include:[10]

- Chronic lymphocytic leukaemia (CLL): As a single agent or in combination with rituximab or obinutuzumab for the treatment of adult patients with previously untreated CLL, and as a single agent or in combination with bendamustine and rituximab (BR) for the treatment of adult patients with CLL who have received at least one prior therapy
- Mantle cell lymphoma (MCL): As a single agent for the treatment of adult patients with relapsed or refractory MCL
- Waldenström's macroglobulinemia (WM): As a single agent for the treatment of adult patients who have received at least one prior therapy or in first-line treatment for patients unsuitable for chemo-immunotherapy, and in combination with rituximab for the treatment of adult patients

Ibrutinib is approved in more than 100 countries for at least one indication, and to date, has been used to treat more than 200,000 patients worldwide.[13]

For a full list of side effects and information on dosage and administration, contraindications and other precautions when using ibrutinib please refer to the Summary of Product Characteristics for further information.

About Chronic Lymphocytic Leukaemia

Chronic lymphocytic leukaemia (CLL) is typically a slow-growing blood cancer of the white blood cells.[14] The overall incidence of CLL in Europe is approximately 4.92 cases per 100,000 persons per year and is about 1.5 times more common in men than in women.[15] CLL is predominantly a disease of the elderly, with a median age of 72 years at diagnosis.[16]

The disease eventually progresses in the majority of patients, and they are faced with fewer treatment options with each relapse. Patients are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension. Learn more at www.janssen.com/emea. Follow us at www.twitter.com/janssenEMEA for our latest news. Janssen Biotech, Inc.; Janssen-Cilag Ltd., Middle East; and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of ibrutinib. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialise, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV and/or any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behaviour and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 29, 2019, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. Neither the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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