Media & Investor Release

Roche announces positive data from broad blood cancer portfolio at European Hematology Association Annual Meeting

- **Long-term data at the European Hematology Association (EHA) 2022 congress expands understanding of the impact of Roche medicines in early-stage blood cancers with the goal of providing patients with robust and durable outcomes from their first treatment**
- **Updated data from phase III CLL14 study of Venclexta®/Venclyxto® (venetoclax) plus Gazyva®/Gazyvaro® (obinutuzumab) showed more than 60% of previously untreated people with chronic lymphocytic leukaemia remained in remission five years after starting treatment[1]**
- **Final analysis of phase III GALLIUM study showed meaningful improvement in progression-free survival was maintained with Gazyva/Gazyvaro plus chemotherapy in people with previously untreated follicular lymphoma after eight years of follow-up[2]**

Basel, 10 June 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that it is presenting new long-term follow-up results and subanalyses from clinical trials of its approved therapies, as well as data on investigational medicines from its broad blood cancer portfolio, at the European Hematology Association (EHA) 2022 Congress in Vienna. Data include five-year results from the phase III CLL14 study of fixed-duration Venclexta®/Venclyxto® (venetoclax) plus Gazyva®/Gazyvaro® (obinutuzumab) in previously untreated chronic lymphocytic leukaemia (CLL); the final analysis of the phase III GALLIUM study of Gazyva/Gazyvaro plus chemotherapy in people with previously untreated advanced-stage follicular lymphoma (FL); and subanalyses from the phase III POLARIX study of Polivy® (polatuzumab vedotin) in combination with MabThera®/Rituxan® (rituximab) plus cyclophosphamide, doxorubicin and prednisone (R-CHP) in people with previously untreated diffuse large B-cell lymphoma (DLBCL). Roche will also present data from its T-cell engaging bispecific antibody development programmes including Lunsumio® (mosunetuzumab) and glofitamab in patients receiving later lines of therapy for non-Hodgkin lymphoma (NHL) and investigational medicines cevostamab and RG6234 in relapsed or refractory (R/R) multiple myeloma (MM).

“Blood cancers remain challenging to treat at all stages, but by improving frontline treatment options we aim to increase the likelihood of meaningful clinical outcomes for these patients,” said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development. “With these new long-term data and other studies of fixed-duration therapies in our portfolio, we are working to lessen the treatment burdens associated with long-term cancer care.”

Improving clinical outcomes with effective frontline treatment options

Five-year results of phase III CLL14 study of Venclexta/Venclyxto plus Gazyva/Gazyvaro (Abstract #S148)

After a median of 65.4 months following treatment with Venclexta/Venclyxto plus Gazyva/Gazyvaro, results confirm the combination continues to be an effective fixed-duration and chemotherapy-free option for patients with previously untreated CLL and coexisting conditions. The estimated investigator-assessed progression-free survival (PFS) rate at this follow-up was 62.6% with Venclexta/Venclyxto plus Gazyva/Gazyvaro and 27.0% with Gazyva/Gazyvaro plus chlorambucil, and the estimated overall survival (OS) rate was 81.9% versus 77.0% (HR 0.72; 95% CI: 0.48-1.09; p=0.12). In addition, the analysis found that 72.1% of patients in the Venclexta/Venclyxto plus Gazyva/Gazyvaro arm did not require another treatment for CLL in the five years following initial treatment (HR 0.42; 95% CI: 0.31-0.57; p<0.0001). No new safety signals were observed.[1] The CLL14 study is being conducted in cooperation with the German CLL Study Group, headed by Michael Hallek, M.D., University of Cologne.

Final analysis of phase III GALLIUM study of Gazyva/Gazyvaro (Abstract #S206)

After eight years of follow-up in people with previously untreated FL, a meaningful improvement in PFS was maintained with Gazyva/Gazyvaro plus chemotherapy, confirming its role as a standard of care for first-line treatment. Seven-year investigator-assessed PFS was significantly improved with Gazyva/Gazyvaro plus chemotherapy (63.4%) compared with MabThera/Rituxan plus chemotherapy (55.7%; HR 0.77; 95% CI: 0.64-0.93; p=0.006). This translated into a longer time to next anti-lymphoma treatment. At seven years, 74.1% of patients receiving Gazyva/Gazyvaro plus chemotherapy had not started new anti-lymphoma therapy compared to 65.4% receiving MabThera/Rituxan plus chemotherapy (HR 0.71; 95% CI: 0.58–0.87; p=0.001). The incidence of serious adverse events was 48.9% with Gazyva/Gazyvaro plus chemotherapy and 43.4% with MabThera/Rituxan plus chemotherapy.[2]

Subgroup analyses of pivotal phase III POLARIX study (Abstract #P1192)

Exploratory subgroup analyses of the phase III POLARIX study of Polivy with R-CHP compared to the current standard of care, MabThera/Rituxan plus cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP), in people with previously untreated DLBCL further support the potential for Polivy to transform the standard of care for people with this aggressive type of lymphoma. One of the datasets being presented is an analysis of study participants from Asia (China, Hong Kong, Japan, South Korea and Taiwan). Among this subgroup, results showed a significant improvement in PFS with Polivy plus R-CHP versus R-CHOP, reducing the risk of disease progression, relapse or death by 36% (HR 0.64; 95% CI: 0.40-1.03). The safety profile was generally comparable for both regimens.[3]

Based on the positive POLARIX results from the overall study population, the European Commission (EC) approved Polivy plus R-CHP in May 2022 for the treatment of adult patients with previously untreated DLBCL.

Providing novel bispecific antibodies for patients receiving later lines of therapy in lymphoma and beyond

Pivotal data from phase II NP30179 expansion study of glofitamab (Abstract #S220)

The pivotal phase II NP30179 expansion study included patients with heavily pre-treated and highly refractory DLBCL and showed fixed-duration glofitamab, an investigational CD20xCD3 T-cell engaging bispecific antibody, induced high and durable complete response (CR) rates. After a median follow-up of 12.6 months, 39.4% of patients (n=61/155) achieved a CR (primary efficacy endpoint) and half of them (51.6%; n=80/155) achieved an overall response (the percentage of patients with a partial or CR; secondary efficacy endpoint), as assessed by an independent review committee. Cytokine release syndrome (CRS) was the most common adverse event, occurring in 63.0% of patients.[4] These data were recently presented at the American Society of Clinical Oncology 2022 Annual Meeting and have been submitted for approval to the European Medicines Agency (EMA). Submissions to additional health authorities worldwide, including the U.S. Food and Drug Administration (FDA), are planned this year.

Subgroup analysis and Lunsumio retreatment from pivotal phase II GO29781 study (Abstracts #P1126 and #P1124)

An exploratory subgroup analysis showed Lunsumio could be an efficacious and tolerable option in patients aged <65 and ≥65 years who had R/R FL and had received two or more prior therapies. Patients ≥65 years old achieved a higher objective response rate (ORR) than those <65 years old (87.0% vs 77.0%, respectively). Lower rates of CRS and serious adverse events were observed in patients ≥65 years old (37%) compared to those <65 years old (52%).[5] Additional data from the GO29781 study showed that retreatment with Lunsumio in patients who achieved a CR but whose disease subsequently progressed was effective and the safety of retreatment was consistent with initial treatment.[6]

The EC recently approved Lunsumio for the treatment of people with R/R FL who have received at least two prior systemic therapies.

The data being presented at EHA, as well as phase III studies currently underway, will expand the understanding of glofitamab and Lunsumio and their impact in both later and earlier lines of treatment, with the aim of providing robust and durable treatment outcomes for people with different types of lymphomas.

Early data from novel investigational bispecific antibodies in R/R MM (Abstracts #P962 and #S180)

In line with Roche's commitment to improving outcomes and personalising care for people with blood cancer, the company has expanded beyond lymphoma and leukaemia, evaluating two investigational medicines in MM. This is the third most common type of blood cancer, diagnosed in more than 170,000 people around the world each year and involves plasma cells (antibody-producing cells in the bone marrow).[7,8] Although advances in treatment have improved outcomes, MM remains an incurable disease characterised by multiple relapses, with an overall five-year survival rate of about 55%.[9] Roche is presenting data at EHA on cevostamab, an investigational FcRH5xCD3 T-cell engaging bispecific antibody that is being evaluated as a monotherapy and in combination with other medicines to treat people with R/R MM, and on RG6234, a novel GPRC5DxCD3 T-cell engaging bispecific antibody that is being studied in a phase I trial in people with R/R MM. While early, the clinical activity and safety profiles observed with these molecules look encouraging and support further exploration.[10,11]

About Venclexta®/Venclyxto® (venetoclax)

Venclexta/Venclyxto is a first-in-class targeted medicine designed to selectively bind and inhibit the B-cell lymphoma-2 (BCL-2) protein. In some blood cancers and other tumours, BCL-2 builds up and prevents cancer cells from dying or self-destructing, a process called apoptosis. Venclexta/Venclyxto blocks the BCL-2 protein and works to help restore the process of apoptosis.

Venclexta/Venclyxto is being developed by AbbVie and Roche. It is jointly commercialised by AbbVie and Genentech, a member of the Roche Group, in the US and commercialised by AbbVie outside of the US. Together, the companies are committed to research with Venclexta/Venclyxto, which is currently being studied in clinical trials across several types of blood cancers.

In the US, Venclexta has been granted six Breakthrough Therapy Designations by the U.S. Food and Drug Administration: one for previously untreated chronic lymphocytic leukaemia (CLL), two for relapsed or refractory CLL, two for previously untreated acute myeloid leukaemia, and one for myelodysplastic syndromes.

About Gazyva®/Gazyvaro® (obinutuzumab)

Gazyva/Gazyvaro is an engineered monoclonal antibody designed to attach to CD20, a protein found only on certain types of B-cells. It is thought to work by attacking targeted cells both directly and together with the body's immune system. Gazyva/Gazyvaro is part of a collaboration between Roche and Biogen.

In the US, Europe and multiple other countries, Gazyva/Gazyvaro is currently approved in combination with chlorambucil for patients with previously untreated chronic lymphocytic leukaemia (CLL). It is also approved in combination with bendamustine, followed by Gazyva/Gazyvaro maintenance for the treatment of follicular lymphoma (FL) patients who did not respond to a MabThera®/Rituxan® (rituximab)-containing regimen, or whose FL returned after such treatment and in combination with chemotherapy for previously untreated advanced FL.

Additional combination studies investigating Gazyva/Gazyvaro with other approved or investigational medicines, including cancer immunotherapies and small molecule inhibitors, are underway across a range of blood cancers.

About Polivy® (polatuzumab vedotin)

Polivy is a first-in-class anti-CD79b antibody-drug conjugate (ADC). The CD79b protein is expressed specifically in the majority of B-cells, an immune cell impacted in some types of non-Hodgkin lymphoma (NHL), making it a promising target for the development of new therapies.[12,13] Polivy is designed to bind to CD79b and destroys these B-cells through the delivery of an anti-cancer agent, which is thought to minimise the effects on normal cells.[14,15] Polivy is being developed by Roche using Seagen ADC technology and is currently being investigated for the treatment of several types of NHL.

About Roche's investigational CD20xCD3 bispecifics in haematology

Roche is currently developing two CD20xCD3 T-cell engaging bispecific antibodies, Lunsumio® (mosunetuzumab) and glofitamab, designed to target CD20 on the surface of B-cells and CD3 on the surface of T-cells. This dual targeting activates and redirects a patient's existing T-cells to engage and eliminate target B-cells by releasing cytotoxic proteins into the B-cells. Lunsumio and glofitamab differ in their structures, and both are being developed by Roche as part of our ongoing strategy to explore multiple bispecific formats in order to identify those that maximise potential clinical benefits for patients. Lunsumio has a structure similar to that of a natural human antibody in that it has two 'Fab' regions but is different from naturally-occurring antibodies in that one 'Fab' region targets CD20 and the other 'Fab' region targets CD3. Glofitamab is based on a novel structural format that we call '2:1,' which refers to the structure of the antibody. It is engineered to have two 'Fab' regions that bind to CD20 and one 'Fab' region that binds to CD3. The clinical development programmes for Lunsumio and glofitamab include ongoing investigations of these molecules as monotherapies and in combination with other medicines for the treatment of people with CD20-positive B cell non-Hodgkin lymphomas, including diffuse large B-cell lymphoma and follicular lymphoma.

About Roche

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

In recognising our endeavor to pursue a long-term perspective in all we do, Roche has been named one of the most sustainable companies in the pharmaceuticals industry by the Dow Jones Sustainability Indices for the thirteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan.

For more information, please visit www.roche.com.

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