SANOFI

Media Update

# CHMP recommends approval of Sarclisa® (isatuximab) in combination with carfilzomib and dexamethasone for the treatment of relapsed multiple myeloma

- CHMP issues positive opinion for second indication for Sarclisa in combination with carfilzomib and dexamethasone for adult patients with multiple myeloma who have received at least one prior therapy
- Recommendation based on data from Phase 3 IKEMA study in which Sarclisa combination therapy demonstrated a statistically significant improvement of progression free survival compared to standard of care carfilzomib and dexamethasone
- Multiple myeloma remains an incurable cancer, despite available treatment options, associated with significant patient burden

**February 26, 2021**

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion for a second indication for Sarclisa® (isatuximab), in combination with carfilzomib and dexamethasone (Kd), for the treatment of adult patients with multiple myeloma (MM) who have received at least one prior therapy.

> *"Sarclisa has demonstrated superior results in combination with two standard of care regimens, reinforcing its potential to become the anti-CD38 of choice for the treatment of multiple myeloma," said Peter Adamson, Global Development Head, Oncology and Pediatric Innovation at Sanofi. "We look forward to partnering with the European Commission to make Sarclisa available to more patients and are committed to investigating Sarclisa in combination with current standard of care treatments throughout all lines of multiple myeloma therapy."*

Sarclisa is currently approved for use in the European Union (EU) in combination with pomalidomide and dexamethasone for the treatment of adult patients with relapsed and refractory MM who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on the last therapy.

The use of Sarclisa in combination with carfilzomib and dexamethasone is not currently approved in the EU, but the final decision whether to expand the indication is expected from the European Commission in the coming months.

## Sarclisa Phase 3 study results in patients with MM

The CHMP positive opinion is based on data from the Phase 3 IKEMA study, a randomized, multi-center, open label clinical trial that enrolled 302 patients with relapsed multiple myeloma across 69 centers spanning 16 countries. The primary endpoint of IKEMA was progression free survival (PFS). While median PFS, defined as time to disease progression or death, for Kd was 19.15 months, the median PFS for patients receiving Sarclisa added to carfilzomib and dexamethasone (Sarclisa combination therapy; n=179) had not been reached at the time of the pre-planned interim analysis. Sarclisa combination therapy reduced the risk of disease progression or death by 47% (hazard ratio 0.531, 99% CI 0.318-0.889, p=0.0007) versus standard of care Kd alone in patients with MM.

Secondary endpoints of the IKEMA trial assessed the depth of response for Sarclisa combination therapy compared to Kd, including overall response rate (ORR), complete response (CR), very good partial response (VGPR) and minimal residual disease (MRD)-negative response. There was no statistically significant difference in ORR, which remained similar for each arm at 86.6% for the Sarclisa combination therapy versus 82.9% for Kd (p=0.1930). The rate of CR was 39.7% in the Sarclisa combination therapy arm and 27.6% in the Kd arm. The rate of VGPR was 72.6% for patients receiving Sarclisa combination therapy and 56.1% for patients receiving Kd. MRD-negative complete response was observed in 29.6% of patients in the Sarclisa combination therapy arm versus 13% of patients in the Kd arm, indicating that nearly 30% of patients treated with Sarclisa combination therapy achieved undetectable levels of MM at $10^{-5}$ sensitivity as measured by next generation sequencing (NGS). At the time of the interim analysis, overall survival (OS) data were still immature.

The most frequent adverse reactions (≥20%) were infusion reactions (45.8%), hypertension (36.7%), diarrhea (36.2%), upper respiratory tract infection (36.2%), pneumonia (28.8%), fatigue (28.2%), dyspnea (27.7%), insomnia (23.7%), bronchitis (22.6%), and back pain (22.0%). Serious adverse reactions occurred in 59.3% of patients receiving Sarclisa combination therapy and versus 57.4% in patients receiving Kd. The most frequent serious adverse reaction was pneumonia (21.5%). Permanent discontinuation of treatment because of adverse reactions was reported in 8.5% of patients treated with Sarclisa combination therapy and in 13.9% of patients treated with Kd. Fatal adverse events were reported in 3.4% of patients treated with Sarclisa combination therapy and in 1.6% of patients treated with Kd.

## Multiple Myeloma: An incurable cancer, despite available treatments

Multiple myeloma is the second most common hematologic malignancy[1], with more than 130,000 new diagnoses of multiple myeloma worldwide yearly.[2] In Europe, approximately 39,000 patients are diagnosed with multiple myeloma each year.[3] Despite available treatments, multiple myeloma remains an incurable malignancy, and is associated with significant patient burden. Since multiple myeloma does not have a cure, most patients will relapse. Relapsed multiple myeloma is the term for when the cancer returns after

treatment or a period of remission. Refractory multiple myeloma refers to when the cancer does not respond or no longer responds to therapy.

## About Sarclisa

Sarclisa is a monoclonal antibody that binds to a specific epitope on the CD38 receptor on MM cells. It is designed to work through multiple mechanisms of action including programmed tumor cell death (apoptosis) and immunomodulatory activity. CD38 is highly and uniformly expressed on the surface of MM cells, making it a potential target for antibody-based therapeutics such as Sarclisa.

Sarclisa is approved in the EU, U.S., Switzerland, Canada, Australia, Japan, Russia, the UAE, South Korea and Taiwan in combination with pom-dex for the treatment of certain adults with relapsed refractory MM. In the U.S., the generic name for Sarclisa is isatuximab-irfc, with irfc as the suffix designated in accordance with Nonproprietary Naming of Biological Products Guidance for Industry issued by the U.S. Food and Drug Administration.

Sarclisa continues to be evaluated in multiple ongoing Phase 3 clinical trials in combination with current standard treatments across the MM treatment continuum. It is also under investigation for the treatment of other hematologic malignancies and solid tumors. The safety and efficacy of these additional uses have not been reviewed by any regulatory authority worldwide.

For more information on Sarclisa clinical trials please visit www.clinicaltrials.gov.

**About Sanofi**

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

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***Sanofi Forward-Looking Statements***

*This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that COVID-19 will have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. Any material effect of COVID-19 on any of the foregoing could also adversely impact us. This situation is changing rapidly and additional impacts may arise of which we are not currently aware and may exacerbate other previously identified risks. The risks and uncertainties also include the uncertainties discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2019. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.*

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[1] Kazandjian. Multiple myeloma epidemiology and survival: A unique malignancy. Semin Oncol. 2016;43(6):676-681. doi:10.1053/j/seminoncol.2016.11.004

[2] International Myeloma Foundation. Myeloma Action Month. https://mam.myeloma.org/learn-more-about-multiple-myeloma/. Accessed February 2021. 2/6.

[3] João C, Costa C, Coelho I, Vergueiro MJ, Ferreira M, Silva MG. Long-term survival in multiple myeloma. Clinical Case Reports. 2014;2(5):173-179. doi:10.1002/ccr3.76. 3. Schey SA, Morris J, Maguire Á, Dhanasiri