Press Release

Sarclisa approved in the US as the first anti-CD38 therapy in combination with standard-of-care treatment for adult patients with newly diagnosed multiple myeloma not eligible for transplant

- Approval based on positive results from the IMROZ phase 3 study demonstrating Sarclisa in combination with bortezomib, lenalidomide, and dexamethasone (VRd) significantly improved progression-free survival (PFS), compared to standard-of-care in newly diagnosed adult patients not eligible for autologous stem cell transplant (ASCT)
- Third indication for Sarclisa, evaluated under FDA Priority Review, underscores Sanofi's commitment to helping close a critical care gap in multiple myeloma (MM)

PARIS, September 21, 2024. The US Food and Drug Administration (FDA) has approved Sarclisa (isatuximab) in combination with bortezomib, lenalidomide, and dexamethasone (VRd) as a first line treatment option for adult patients with newly diagnosed multiple myeloma (NDMM) who are not eligible for autologous stem cell transplant (ASCT). Sarclisa is the first anti-CD38 therapy in combination with standard-of-care VRd to significantly reduce disease progression or death (by 40%) compared to VRd alone for patients with NDMM not eligible for transplant.

> ***Thomas Martin M.D.***
> Helen Diller Family Comprehensive Cancer Center Clinical Professor of Medicine at the University of California San Francisco
> *"Multiple myeloma is most frequently diagnosed in patients 65 years and older, yet the options for treatment in this population are limited due to a combination of age, frailty, and co-morbidities. This has resulted in a longstanding need for new treatment options that can potentially improve the standard-of-care. The significant clinical benefit and improvements in progression-free survival demonstrated by the IMROZ regimen of isatuximab plus VRd versus VRd alone make today's approval an important moment for this vulnerable patient population and the larger multiple myeloma community."*

This decision marks the third approved indication for Sarclisa in the US and the first approved indication in newly diagnosed patients. The FDA evaluated Sarclisa for this indication under Priority Review, which is reserved for medicines that represent potentially significant improvements in efficacy or safety in treating serious conditions. Sarclisa is also currently approved in more than 50 countries across two indications for the treatment of people with relapsed or refractory disease.

> ***Brian Foard***
> Executive Vice President, Head of Specialty Care, Sanofi
> *"Since first launching in 2020, we have made significant progress towards our ambition of establishing Sarclisa as a best-in-class therapy. The FDA's decision marks another momentous milestone toward our goal and expands the reach of this potentially transformative therapy to a larger population. With today's approval, doctors now have an important new option at their disposal that's been shown to slow disease progression for longer compared to the current standard-of-care for adults living with newly diagnosed multiple myeloma who are not eligible for transplant in the US."*

Results from the IMROZ phase 3 study supporting Sarclisa in NDMM not eligible for ASCT

The FDA approval is based on data from the IMROZ phase 3 study recently presented at the American Society of Clinical Oncology (ASCO) 2024 annual meeting and published in *The New England Journal of Medicine*. IMROZ is the first global phase 3 study of an anti-CD38 monoclonal

antibody in combination with standard-of-care VRd to significantly improve PFS versus VRd alone.

In the IMROZ study, Sarclisa-VRd followed by Sarclisa-Rd met the primary endpoint of PFS, significantly reducing the risk of recurrence or death by 40%, compared to VRd followed by Rd, in patients with NDMM not eligible for ASCT (HR 0.60; 95% CI: 0.44 to 0.81, p=0.0009). At a median follow-up of 59.7 months, the median PFS with the Sarclisa-VRd combination was not reached versus 54.3 months with VRd. The estimated PFS-rate at 60 months was 63.2% for patients treated with Sarclisa-VRd versus 45.2% for VRd.

Sarclisa-VRd also met several secondary endpoints which demonstrated deep responses in this patient population:

- Approximately three-quarters (74.7%) of patients treated with Sarclisa-VRd achieved a complete response (CR) or better compared to 64.1% of patients taking VRd (OR 1.7; 95% CI: 1.097-2.5; p=0.0160).
- More than half (55.5%) of patients treated with Sarclisa-VRd achieved MRD negative CR compared to 40.9% of patients taking VRd (OR 1.8; 95% CI: 1.229-2.646; p=0.0026).

The safety and tolerability of Sarclisa observed in this study was consistent with the established safety profile of Sarclisa and VRd with no new safety signals observed. The most common adverse reactions (≥20%) were upper respiratory tract infections, diarrhea, fatigue, peripheral sensory neuropathy, pneumonia, musculoskeletal pain, cataract, constipation, peripheral edema, rash, infusion-related reaction, insomnia, and COVID-19. The most common hematologic laboratory abnormalities (≥80%) were decreased hemoglobin, decreased leukocytes, decreased lymphocytes, decreased platelets, and decreased neutrophils. Serious adverse reactions occurred in 71% of patients receiving Sarclisa combination therapy. The most frequent serious adverse reaction occurring in more than 5% of patients was pneumonia (30%). Permanent discontinuation of treatment due to an adverse reaction occurred in 22.8% of patients treated with Sarclisa combination therapy, compared to 26% in the comparator arm.

Advancing Sarclisa in multiple myeloma

Sanofi continues to advance Sarclisa as part of a patient-centric clinical development program, which includes several phase 2 and phase 3 studies across the MM treatment continuum spanning six potential indications. In addition, the company is evaluating a subcutaneous administration method for Sarclisa in clinical studies. The safety and efficacy of Sarclisa has not been evaluated by any regulatory authority outside of its approved indications and methods of delivery.

In September, isatuximab-irfc (Sarclisa) was also added to the National Comprehensive Cancer Network (NCCN®) Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for MM non-transplant candidates as an NCCN Category 1 Preferred option in combination with VRd for patients <80 years old who are not frail. Category 1 is based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. Preferred intervention are interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.

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About Sarclisa

Sarclisa (isatuximab) is a monoclonal antibody that binds to a specific epitope on the CD38 receptor on MM cells, inducing distinct antitumor activity. 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 target for antibody-based therapeutics such as Sarclisa.

Based on the ICARIA-MM phase 3 study, Sarclisa is approved in more than 50 countries, including the US and the EU, in combination with pomalidomide and dexamethasone for the

treatment of patients with relapsed refractory MM (RRMM) who have received ≥2 prior therapies, including lenalidomide and a proteasome inhibitor and who progressed on last therapy. Based on the IKEMA phase 3 study, Sarclisa is also approved in 50 countries in combination with carfilzomib and dexamethasone, including in the US for the treatment of patients with RRMM who have received 1–3 prior lines of therapy and in the EU for patients with MM who have received at least one prior therapy. In the US, the non-proprietary 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 US Food and Drug Administration.

Sarclisa continues to be evaluated in multiple ongoing phase 3 clinical studies in combination with current standard treatments across the MM treatment continuum. It is also under investigation for the treatment of other hematologic malignancies, and its safety and efficacy have not been evaluated by any regulatory authority outside of its approved indication.

Sanofi is committed to pursuing the advancement of Sarclisa through several investigational studies across the MM treatment continuum. Various patient-centric clinical development programs aim to bring Sarclisa to more patients, intercept the disease earlier in the treatment journey, explore potential new combinations and assess subcutaneous administration via a proprietary on body device system. The safety and efficacy of Sarclisa has not been evaluated by any regulatory authority outside of its approved indications and methods of delivery.

In striving to become the number one immunoscience company globally, Sanofi remains committed to advancing oncology innovation. Through focused strategic decisions the company has reshaped and prioritized its pipeline, leveraging its expertise in immunoscience to drive progress. Efforts are centered on difficult-to-treat cancers such as select hematologic malignancies, and solid tumors with critical unmet needs, including multiple myeloma, acute myeloid leukemia, certain types of lymphomas, as well as gastrointestinal and lung cancers.

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

About multiple myeloma

MM is the second most common hematologic malignancy[1], affecting more than 130,000 patients in the US; approximately 32,000 Americans are diagnosed with MM each year.[2] Despite available treatments, MM remains an incurable malignancy with an estimated 52% five-year survival rate for newly diagnosed patients.[3] According to physician-based surveys, the majority of NDMM patients are not considered eligible for transplant, creating a need for new frontline therapeutic options, particularly due to high attrition rates in subsequent lines of therapy.

About Sanofi

We are an innovative global healthcare company, driven by one purpose: we chase the miracles of science to improve people's lives. Our team, across the world, is dedicated to transforming the practice of medicine by working to turn the impossible into the possible. We provide potentially life-changing treatment options and life-saving vaccine protection to millions of people globally, while putting sustainability and social responsibility at the center of our ambitions.

Sanofi is listed on EURONEXT: SAN and NASDAQ: SNY

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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 regarding the marketing and other potential of the product, or regarding potential future revenues from the product. 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, unexpected regulatory actions or delays, or government regulation generally, that could affect the availability or commercial potential of the product, the fact that product may not be commercially successful, the uncertainties inherent in research and development, including future clinical data and analysis of existing clinical data relating to the product, including post marketing, unexpected safety, quality or manufacturing issues, competition in general, risks associated with intellectual property and any related future litigation and the ultimate outcome of such litigation, and volatile economic and market conditions, and the impact that pandemics or other global crises may 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. 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, 2023. 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.
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[3] Fonseca, R., Usmani, S.Z., Mehra, M. et al. Frontline treatment patterns and attrition rates by subsequent lines of therapy in patients with newly diagnosed multiple myeloma. *BMC Cancer*. 2020: 20(1087). https://doi.org/10.1186/s12885-020-07503-y.