Press Release

ASCO: new Sarclisa data support subcutaneous administration with on-body injector

- New data from two clinical studies demonstrated that Sarclisa administered subcutaneously via an investigational on-body injector shortened treatment time to minutes with similar efficacy and safety compared to intravenous infusion
- Studies used Enable Injections' enFuse® on-body injector, an automated hands-free injector
- Data will form the basis of global regulatory submissions across all currently approved lines of treatment

Paris, June 3, 2025. New data from two clinical studies of the investigational use of Sarclisa administered subcutaneously (SC) via an on-body injector (OBI) (also referred to as an on-body delivery system) in relapsed or refractory multiple myeloma (R/R MM) support the potential use of this innovative delivery method to advance patient care, while upholding Sarclisa's efficacy and safety profile. The results were presented at the American Society of Clinical Oncology (ASCO) Annual Meeting and include full data from the IRAKLIA phase 3 study, the first to incorporate the use of an OBI in the treatment of MM, and demonstrate non-inferior efficacy and pharmacokinetics compared to Sarclisa intravenous (IV) infusion.

> ***Alyssa Johnsen, MD, PhD***
> Global Therapeutic Area Head, Immunology and Oncology Development
> *"Our subcutaneous clinical program is rooted in our mission to address patient needs and reduce treatment burden in multiple myeloma. We believe the novel on-body injector represents a significant innovation that could improve and streamline the treatment process for both patients and providers. We are pleased to share these data, the first to evaluate an on-body injector with a multiple myeloma treatment, and look forward to potentially bringing this formulation and administration option to the multiple myeloma community."*

The OBI offers the potential to improve the overall patient experience in MM treatment. Recent studies and surveys suggest the use of an OBI may be associated with greater convenience, flexibility, and patient satisfaction compared to IV or manual SC administration methods.[1] In addition, an OBI may also streamline the administration process for providers, potentially reducing the physical burden on nurses and enabling them to possibly move freely through the use of a hands-free device while monitoring the patient during injection.

The IRAKLIA phase 3 study and the IZALCO phase 2 study presented at ASCO were conducted using Enable Injections' enFuse® hands-free OBI, an automated injector designed to subcutaneously administer high-volume medicines beginning with the click of a button, to administer the hyaluronidase-free SC formulation of Sarclisa. The enFuse device uses a 30 gauge, hidden, and retractable needle that is smaller compared to some of the commonly used large-volume SC injection needles, which may support patient comfort.

The safety and efficacy of Sarclisa SC administered with the OBI or manual administration are investigational and have not been approved for use by any regulatory authority.

IRAKLIA phase 3 study

IRAKLIA is a global, randomized, open-label, pivotal phase 3 non-inferiority study comparing Sarclisa SC administered via an OBI and Sarclisa IV, both in combination with pomalidomide and dexamethasone (Pd) in adult patients with R/R MM who have received at least one prior line of treatment. At the data cut-off of November 6, 2024, and a median follow-up of 12 months, the study demonstrated:

Primary endpoints

- **Objective response rate (ORR) with Sarclisa SC-Pd was 71.1%** compared to 70.5% with Sarclisa IV-Pd, establishing non-inferiority (risk ratio [RR] 1.008; 95% confidence interval [CI]: 0.903-1.126; p=0.0006).
- **Observed Sarclisa mean (standard deviation [SD]) concentration before dosing (C trough) at steady state (C6D1 pre-dose) with Sarclisa SC-Pd was 499 (259) ug/mL** compared to 341 (169) ug/mL with Sarclisa IV-Pd, establishing non-inferiority (geometric mean ratio [GMR] 1.532; 90% CI: 1.316-1.784).

Secondary endpoints

- **Very good partial response (VGPR) or better rates were consistent** between Sarclisa SC-Pd and Sarclisa IV-Pd at 46.4% and 45.9%, respectively (RR 1.011; 95% CI: 0.841-1.215; p<0.0001).
- **Observed Sarclisa mean (SD) C trough at 4 weeks (C2D1 pre-dose) with Sarclisa SC-Pd was 421 (215) ug/mL** compared to 302 (117) ug/mL with Sarclisa IV-Pd (GMR 1.302; 90% CI 1.158-1.465).
- **Systemic infusion reactions (IR) were significantly lower with Sarclisa SC-Pd,** occurring in only 1.5% of patients compared to 25% of those treated with Sarclisa IV-Pd (RR: 0.061; 95% CI: 0.022-0.164; p<0.0001). Of note, nearly all IRs occurring were grade 1 or 2 and resolved within one day. No patients in the Sarclisa SC-Pd arm discontinued treatment due to a systemic IR.
- **Most Sarclisa SC-Pd-treated patients (70%) reported being satisfied or very satisfied with their injection** compared to 53.4% in the Sarclisa IV-Pd arm, demonstrating the positive impact of this innovative method of administration on the patient experience (OR 2.036; 95% CI: 1.425-2.908; p=0.0001).
- **99.9% of Sarclisa SC OBI injections were successfully delivered** with no significant safety concerns related to the OBI.
- **Progression-free survival (PFS) rates at 12 months were also similar,** reaching 66.1% for patients treated with Sarclisa SC-Pd compared to 65.1% of patients treated with Sarclisa IV-Pd (HR 0.985; 95% CI: 0.726-1.338).

The overall safety profile of Sarclisa SC-Pd observed in this study was consistent with the established safety profile of Sarclisa IV-Pd, but with a notably lower rate of systemic IRs. No new safety concerns were observed, except for low-grade local injection site reactions (ISRs) associated with SC administration that occurred with a low incidence (0.4%, n=19/5,145 injections). Nearly all ISRs were grade 1, except for one episode of grade 2.

> ***Xavier Leleu, MD, PhD***
> Head of the Department of Hematology and Myeloma Clinic at the Hôpital La Mileterie and study investigator
> *"Results from the IRAKLIA phase 3 study represent a potentially transformational advancement in the administration of multiple myeloma treatment. These data not only establish non-inferiority between Sarclisa administered both subcutaneously and intravenously across several key endpoints but reinforce the positive impact that this on-body injector could have on the patient treatment experience, as demonstrated by patient satisfaction scores."*

In addition to the oral presentation at ASCO, the full data were simultaneously published in the *Journal of Clinical Oncology*.

IZALCO phase 2 study

In addition to the IRAKLIA phase 3 study, Sanofi also presented new data from the randomized, sequential, open-label, IZALCO phase 2 study evaluating the efficacy and safety of Sarclisa SC administered via manual push or an OBI, in combination with carfilzomib and dexamethasone (Kd) in adult patients with R/R MM who have received one to three prior lines of therapy. At a median follow-up of 10.1 months, the study demonstrated:

- **ORR was 79.7% in patients treated with Sarclisa SC-Kd** (95% CI: 68.8-88.2) validating the prespecified efficacy hypothesis.

- With a median follow-up of 10 months, **VGPR or better rate in patients treated with Sarclisa SC-Kd was 62.2% and complete response (CR) or better rate was 21.6%.**
- Only two patients treated with Sarclisa SC-Kd, or 2.7% of recipients, experienced a grade 2 or lower IR event with manual injection and no IR event occurred with OBI administration; approximately 1% of injections were associated with a local ISR.
- After treatment with both methods, **most patients (74.5%) preferred the OBI** versus 17% who preferred manual injection and 8.5% with no preference (p=0.0004; binomial test against the null hypothesis of ≤50% rate).

The overall safety profile of Sarclisa SC-Kd observed in this study was consistent with the established safety profile of Sarclisa IV-Kd, with no new safety concerns observed.

Advancing patient and provider-centric innovation in MM

While SC administration is currently available for certain MM treatment regimens through a manual injection, administering large-volume medicines manually can present significant challenges, including a labor-intensive process for nurses, risk of strain and needlestick injuries, and potential need for larger needles that may compromise patient comfort and increase anxiety.

> ***Mehul Desai, PharmD, MBA***
> Vice President, Medical Affairs, Enable Injections
> *"We believe multiple myeloma patients deserve a more convenient and comfortable treatment experience and recognize the crucial role providers play in delivering that care. Through our collaboration with Sanofi, we've aspired to advance an on-body injector that could transform the treatment experience for patients and providers alike. The results from the IRAKLIA and IZALCO studies represent a significant step toward our ambition and validate the potential of the on-body injector to deliver the same high standard of efficacy established with intravenous Sarclisa."*

In addition to IRAKLIA and IZALCO, Sanofi is also evaluating Sarclisa SC administration via an OBI in the front-line treatment setting. The ISASOCUT phase 2 study conducted by the University of Poitiers, is evaluating Sarclisa in combination with bortezomib, lenalidomide and dexamethasone (VRd) in adult patients with newly diagnosed MM (NDMM) not eligible for autologous stem-cell transplant (ASCT), while the German-speaking Myeloma Multicenter Group (GMMG)-HD8 phase 3 study, conducted in collaboration with the GMMG and the German Multiple Myeloma Study Group Consortium (DSMM), is evaluating Sarclisa SC-VRd induction in NDMM patients who are eligible for ASCT. In addition, results from the IZALCO, IRAKLIA and ISASOCUT studies will be presented at the European Hematology Association Congress later this month. The IRAKLIA abstract was also hand-selected to be included in the 2025 Best of ASCO program, held later in the summer of 2025, following the ASCO Annual Meeting. The data from these studies, collectively, will form the basis for global regulatory submissions.

Sarclisa administered subcutaneously via the on-body injector or manual administration is investigational and has not been approved for any use by any regulatory authority. The safety and efficacy of this formulation and delivery method have not been established.

About the IRAKLIA and IZALCO studies

IRAKLIA is a randomized, open-label, pivotal phase 3 study evaluating the non-inferiority of Sarclisa SC formulation administered at a fixed dose SC via an OBI versus weight-based dosed Sarclisa IV in combination with Pd in adult patients with R/R MM who have received at least one prior line of therapy. The co-primary outcomes being assessed are ORR, defined as the proportion of patients with stringent CR, CR, VGPR, and partial response (PR) according to the 2016 IMWG criteria assessed by Independent Review Committee (IRC), and observed C trough at steady state (pre-dose at C6D1), defined as observed Sarclisa plasma concentrations.

IZALCO is a two-part, randomized, sequential, open-label, phase 2 study evaluating the efficacy and safety of Sarclisa SC formulation administered SC via manual push or an OBI in adult patients with R/R MM who have received one to three prior lines of therapy. The primary objective is ORR, as assessed by IRC. The secondary objective is patient preference for the OBI versus manual administration of Sarclisa SC.

About Enable Injections

Based in the US (Cincinnati, OH), Enable Injections is a global healthcare innovation company committed to improving the patient treatment experience through the development and manufacturing of enFuse. enFuse is an innovative wearable drug delivery platform that is designed to deliver large volumes of pharmaceutical and biologic therapeutics via subcutaneous administration, with the aim of improving convenience, supporting superior outcomes, and advancing healthcare system economics. For more information, visit https://enableinjections.com.

About Sarclisa

Sarclisa (isatuximab) is approved in more than 50 countries, including in the US, EU, Japan, and China, across multiple treatment lines for MM. Based on the ICARIA-MM phase 3 study, Sarclisa is approved in the US, EU and Japan in combination with Pd for the treatment of patients with R/R MM who have received ≥two prior therapies, including lenalidomide and a proteasome inhibitor and have relapsed on the last therapy; this combination is also approved in China for patients who have received at least one prior line of therapy, including lenalidomide and a proteasome inhibitor. Based on the IKEMA phase 3 study, Sarclisa is also approved in more than 50 countries in combination with carfilzomib and dexamethasone, including in the US for the treatment of patients with R/R MM who have received one to three prior lines of therapy and in the EU for patients with MM who have received at least one prior therapy. In the US, EU, UK, and China, Sarclisa is approved in combination with VRd as a front-line treatment option in transplant-ineligible NDMM patients, based on the IMROZ phase 3 study. In Japan, Sarclisa is approved in combination with VRd as a front-line treatment option regardless of transplant eligibility.

At Sanofi, we are building on a long-standing commitment to oncology as we continue to chase the miracles of science to improve the lives of those living with cancer. We are committed to transforming cancer care by developing innovative, first and best-in-class immunological and targeted therapies for rare and difficult-to-treat cancers with high unmet need.

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

About Sanofi

Sanofi is an R&D driven, AI-powered biopharma company committed to improving people's lives and creating compelling growth. We apply our deep understanding of the immune system to invent medicines and vaccines that treat and protect millions of people around the world, with an innovative pipeline that could benefit millions more. Our team is guided by one purpose: we chase the miracles of science to improve people's lives; this inspires us to drive progress and deliver positive impact for our people and the communities we serve, by addressing the most urgent healthcare, environmental, and societal challenges of our time.
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 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, 2024. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.