MoonLake Immunotherapeutics starts Phase 3 IZAR program of the Nanobody® sonelokimab in patients with active psoriatic arthritis

- *Two trials for active psoriatic arthritis (PsA) with one focusing on biologic-naïve patients and including evaluation of radiographic progression (IZAR-1), and the other focusing on TNF-IR patients while being the first trial to include risankizumab as an active reference arm (IZAR-2)*
- *Program will evaluate sonelokimab for a total of 52 weeks, across IZAR-1 and IZAR-2, at sites in the United States, Europe and Latin America, using a design informed by the Phase 2 ARGO trial*
- *The IZAR program builds upon the Phase 3 VELA program for sonelokimab in hidradenitis suppurativa (HS) which started in May*
- *The topline primary endpoint readout at week 16 for the program is expected in H1 2026*

Zug, Switzerland, November 13, 2024 – MoonLake Immunotherapeutics (MoonLake; Nasdaq: MLTX), a clinical-stage biotechnology company focused on creating next-level therapies for inflammatory diseases, today announced that the first patients have been screened at U.S. trial sites in its global Phase 3 clinical program, IZAR, evaluating sonelokimab, an investigational Nanobody® designed to treat inflammatory disease, in patients with active psoriatic arthritis (PsA).

PsA is a chronic, debilitating and progressive inflammatory condition that not only affects the peripheral joints and skin but also other domains such as entheses, nails and axial joints. This multi-domain disease presents with significant unmet needs, especially in managing inflammation and pain across multiple domains simultaneously. Although the exact mechanisms underlying PsA are not fully understood, evidence indicates that activation of the IL-17 pathway plays a crucial role in its pathophysiology. Sonelokimab, a Nanobody®, is designed to directly target sites of inflammation by inhibiting the IL-17A/A, IL-17A/F, and IL-17F/F dimers. Its smaller size as a Nanobody® compared to antibodies allows it to better penetrate and treat difficult-to-reach inflamed tissues.

Following the positive results from the Phase 2 ARGO trial, the Phase 3 IZAR program is expected to enroll approximately 1,500 adult patients across two trials, IZAR-1 (NCT06641076) and IZAR-2 (NCT06641089). The global, randomized, double-blind placebo-controlled IZAR trials are designed to evaluate the efficacy and safety of the Nanobody® sonelokimab over 52 weeks. IZAR-1 will enroll biologic-naïve patients and include an evaluation of radiographic progression, while IZAR-2 will enroll patients with an inadequate response to tumor necrosis factor-α inhibitors (TNF-IR) and will be the first to include risankizumab, a monoclonal antibody that inhibits IL-23, as an active reference arm. The primary endpoint (American College of Rheumatology (ACR) 50) compared to placebo, and key secondary endpoints for both trials are expected to read out at Week 16. The IZAR program will assess 60mg and 120mg doses of sonelokimab. The readout of the primary endpoint for both IZAR-1 and IZAR-2 is anticipated in H1 2026.

Alan Kivitz, MD, MACR, ARGO and IZAR Investigator commented: *"I'm excited to be part of the Phase 3 IZAR program as an investigator, focusing on the Nanobody® sonelokimab for psoriatic arthritis. This initiative marks a crucial advancement in addressing the urgent need for more treatment options for those suffering from this complex and debilitating multi-domain condition. The Phase 2 ARGO trial yielded particularly promising results, with strong responses across multiple domains including joints, skin, and nails. This robust multi-domain efficacy resulted in up to 61% of patients achieving Minimal*

Disease Activity – an important treatment goal that can significantly improve patients' quality of life – by Week 24. The IZAR program seeks to confirm the effectiveness of sonelokimab in treating PsA, with the ultimate goal of helping more patients reach their treatment goals across multiple domains."

Philip J. Mease, MD, Director of Rheumatology Research at the Providence Swedish Medical Center and Clinical Professor at the University of Washington School of Medicine, Seattle, WA, U.S commented: *"MoonLake's Nanobody®, Sonelokimab is designed to precisely target challenging sites of inflammation by integrating Nanobody® innovation with the dual inhibition of IL-17F and IL-17A – a novel and promising clinical approach that may allow enhanced treatment of the multiple domains of PsA compared with conventional antibodies. Sonelokimab has already shown promising outcomes, with robust clinical efficacy observed across key psoriatic arthritis disease domains. The Phase 3 IZAR program is therefore an exciting opportunity to determine whether the novel design of sonelokimab can raise the current treatment bar in psoriatic arthritis."*

Kristian Reich, Founder and Chief Scientific Officer at MoonLake commented: *"This is a major milestone for MoonLake, marking the second Phase 3 program independently initiated by the company this year. The launch of our Phase 3 IZAR program underscores our dedication to advance the field of inflammation and immunology not only in dermatology but also in rheumatology and to provide novel treatment options for patients with high unmet need. We are in full execution mode with our late-stage clinical development plans and look forward to reporting the primary endpoint in H1 2026."*

The initiation of this Phase 3 program follows the announcement in June 2024 of the successful outcome of MoonLake's end-of-Phase 2 interactions with the U.S. Food and Drug Administration (FDA), as well as positive feedback from its interactions with the European Medicines Agency (EMA).

- Ends –

About Psoriatic Arthritis

Psoriatic arthritis (PsA) is a chronic, progressive and complex inflammatory disease that manifests across multiple domains, leading to substantial functional impairment and decreased quality of life. The clinical features of PsA are diverse, comprising both musculoskeletal (peripheral arthritis, spondylitis, dactylitis, and enthesitis) and non-musculoskeletal (skin and nail disease) domains. PsA occurs in up to 30% of patients with psoriasis, most commonly those aged between 30 and 60 years. Although the exact mechanism of disease is not fully understood, evidence suggests that activation of the IL-17 pathway plays an important role in the disease pathophysiology.

About IZAR

IZAR-1 (NCT06641076) and IZAR-2 (NCT06641089) are global, randomized, double-blind, placebo-controlled Phase 3 trials designed to evaluate the efficacy and safety of sonelokimab compared with placebo in a total of approximately 1,500 adults with active PsA, with a primary endpoint of superiority to placebo in ACR 50 response at Week 16. IZAR-1 will enroll biologic-naïve patients and include an evaluation of radiographic progression, while IZAR-2 will enroll patients with an inadequate response to tumor necrosis factor-α inhibitors (TNF-IR) — reflecting patients commonly seen in clinical practice — and will be the first PsA trial to include a risankizumab active reference arm. Both trials will also assess a range of secondary endpoints reflecting the multiple disease manifestations characteristic of PsA. These include skin and nail outcomes, multidomain outcomes, and patient-reported outcome measures such as pain and quality of life assessments.

About Sonelokimab

Sonelokimab (M1095) is an investigational ~40 kDa humanized Nanobody® consisting of three VHH domains covalently linked by flexible glycine-serine spacers. With two domains, sonelokimab selectively binds with high affinity to IL-17A and IL-17F, thereby inhibiting the IL-17A/A, IL-17A/F, and IL-17F/F dimers. A third central domain binds to human albumin, facilitating further enrichment of sonelokimab at sites of inflammatory edema.

Sonelokimab is being assessed in two lead indications, HS and PSA, and MoonLake is pursuing other indications in dermatology and rheumatology.

For HS, sonelokimab is being assessed in the Phase 3 trials, VELA-1 and VELA-2, following the successful outcome of MoonLake's end-of-Phase 2 interactions with the FDA and as well as positive feedback from its interactions with the EMA announced in February 2024. In June 2023, topline results of the MIRA trial (NCT05322473) at 12 weeks showed that the trial met its primary endpoint, the Hidradenitis Suppurativa Clinical Response (HiSCR)75, which is a higher measure of clinical response versus the HiSCR50 measure used in other clinical trials, setting a landmark milestone. In October 2023, the full dataset from the MIRA trial at 24 weeks showed that maintenance treatment with sonelokimab led to further improvements in HiSCR75 response rates and other high threshold clinical and patient relevant outcomes. The safety profile of sonelokimab in the MIRA trial was consistent with previous trials with no new safety signals detected.

For PsA, sonelokimab is being assessed in the Phase 3 trials, IZAR-1 and IZAR-2, following the announcement in March 2024 of the full dataset from the global Phase 2 ARGO trial (M1095-PSA-201) evaluating the efficacy and safety of the Nanobody® sonelokimab over 24 weeks in patients with active PsA. Significant improvements were observed across all key outcomes, including up to 61% of patients treated with sonelokimab achieving an American College of Rheumatology (ACR) 50 response and Minimal Disease Activity (MDA) at week 24. This followed the positive top-line results in November 2023, where the trial met its primary endpoint with a statistically significant greater proportion of patients treated with either sonelokimab 60mg or 120mg (with induction) achieving ACR50 response compared to those on placebo at week 12. All key secondary endpoints in the trial were met for the 60mg and 120mg doses with induction. The safety profile of sonelokimab in the ARGO trial was consistent with previous trials with no new safety signals detected.

A Phase 2 trial is expected to be initiated in 2024 for palmo-plantar pustulosis (PPP), a debilitating inflammatory skin condition affecting a significant number of patients. In addition, in 2024, a Phase 3 trial is expected to be initiated in adolescent HS, a condition that typically manifests at this early stage of a patient's life, and the period in which irreversible damage and inflammatory remission is most critical.

Sonelokimab will also be assessed in seronegative spondyloarthritis with Phase 2 trials in radiographic and non-radiographic axial spondyloarthritis (axSpA) and PsA. The trials are set to incorporate innovative designs that enhance traditional clinical outcomes with contemporary tissue and cellular imaging techniques.

Sonelokimab has also been assessed in a randomized, placebo-controlled Phase 2b trial (NCT03384745) in 313 patients with moderate-to-severe plaque-type psoriasis. High threshold clinical

responses (Investigator's Global Assessment Score 0 or 1, and Psoriasis Area and Severity Index 90/100) were observed in patients with moderate-to-severe plaque-type psoriasis. Sonelokimab was generally well tolerated, with a safety profile similar to the active control, secukinumab (Papp KA, et al. Lancet. 2021; 397:1564-1575).

In an earlier Phase 1 trial in patients with moderate-to-severe plaque-type psoriasis, sonelokimab has been shown to decrease (to normal skin levels) the cutaneous gene expression of pro-inflammatory cytokines and chemokines (Svecova D. J Am Acad Dermatol. 2019;81:196–203).

About Nanobodies®

Nanobodies® represent a new generation of antibody-derived targeted therapies. They consist of one or more domains based on the small antigen-binding variable regions of heavy-chain-only antibodies (VHH). Nanobodies® have a number of potential advantages over traditional antibodies, including their small size, enhanced tissue penetration, resistance to temperature changes, ease of manufacturing, and their ability to be designed into multivalent therapeutic molecules with bespoke target combinations.

The terms Nanobody® and Nanobodies® are trademarks of Ablynx, a Sanofi company.

About Hidradenitis Suppurativa

Hidradenitis suppurativa is a severely debilitating chronic skin condition resulting in irreversible tissue destruction. HS manifests as painful inflammatory skin lesions, typically around the armpits, groin, and buttocks. Over time, uncontrolled and inadequately treated inflammation can result in irreversible tissue destruction and scarring. The disease affects 0.05–4.1% of the global population, with three times more females affected than males. Real-world data in the US indicates that at least 2 million unique patients have been diagnosed with and treated for HS between 2016 and 2023 alone, highlighting a significant unmet need and impact on healthcare systems, and a market opportunity exceeding $10bn by 2035. Onset typically occurs in early adulthood and HS has a profound negative impact on quality of life, with a higher morbidity than other dermatologic conditions. There is increasing scientific evidence to support IL-17A- and IL-17-mediated inflammation as a key driver of the pathogenesis of HS, with other identified risk factors including genetics, cigarette smoking, and obesity.

About MoonLake Immunotherapeutics

MoonLake Immunotherapeutics is a clinical-stage biopharmaceutical company unlocking the potential of sonelokimab, a novel investigational Nanobody® for the treatment of inflammatory disease, to revolutionize outcomes for patients. Sonelokimab inhibits IL-17A and IL-17F by inhibiting the IL-17A/A, IL-17A/F, and IL17F/F dimers that drive inflammation. The company's focus is on inflammatory diseases with a major unmet need, including hidradenitis suppurativa and psoriatic arthritis – conditions affecting millions of people worldwide with a large need for improved treatment options. MoonLake was founded in 2021 and is headquartered in Zug, Switzerland. Further information is available at www.moonlaketx.com.

Cautionary Statement Regarding Forward Looking Statements

This press release contains certain "forward-looking statements" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. Forward-looking statements include, but are not limited to, statements regarding MoonLake's expectations, hopes, beliefs, intentions or strategies

regarding the future including, without limitation, statements regarding: plans for and timing of clinical trials, including the topline primary endpoint readout for the Phase 3 IZAR program, the trial design and patient enrollment across the IZAR-1 and IZAR-2 trials, and the initiation of Phase 2 trials for PPP, adolescent HS, axSpA and PsA, the efficacy and safety of sonelokimab for the treatment of HS and PsA, including in comparison to existing standards or care or other competing therapies, clinical trials and research and development programs and the anticipated timing of the results from those studies and trials. In addition, any statements that refer to projections, forecasts, or other characterizations of future events or circumstances, including any underlying assumptions, are forward looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "possible," "potential," "predict," "project," "should," "would" and similar expressions may identify forward-looking statements, but the absence of these words does not mean that statement is not forward looking.

Forward-looking statements are based on current expectations and assumptions that, while considered reasonable by MoonLake and its management, as the case may be, are inherently uncertain. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Actual results could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, risks and uncertainties associated with MoonLake's business in general and limited operating history, difficulty enrolling patients in clinical trials, state and federal healthcare reform measures that could result in reduced demand for MoonLake's product candidates and reliance on third parties to conduct and support its preclinical studies and clinical trials and the other risks described in or incorporated by reference into MoonLake's Annual Report on Form 10-K for the year ended December 31, 2023 and subsequent filings with the Securities and Exchange Commission.

Nothing in this press release should be regarded as a representation by any person that the forward-looking statements set forth herein will be achieved or that any of the contemplated results of such forward-looking statements will be achieved. You should not place undue reliance on forward-looking statements in this press release, which speak only as of the date they are made and are qualified in their entirety by reference to the cautionary statements herein. MoonLake does not undertake or accept any duty to release publicly any updates or revisions to any forward-looking statements to reflect any change in its expectations or in the events, conditions or circumstances on which any such statement is based.

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