MoonLake initiates three new clinical trials and further expands the portfolio of indications for the Nanobody® sonelokimab

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- New trials in three new indications have been initiated with the Nanobody® sonelokimab: Phase 3 VELA-TEEN trial in adolescent hidradenitis suppurativa (HS), Phase 2 LEDA trial in palmoplantar pustulosis (PPP) and Phase 2 S-OLARIS trial in axial spondyloarthritis (axSpA)
- MoonLake now independently running seven trials in 2025 across large dermatology and rheumatology indications: adult HS, adolescent HS, psoriatic arthritis (PsA), PPP and axSpA
- Phase 2 and Phase 3 data read-outs across all target indications expected in 2025 (adult HS, and PPP) and 2026 (adolescent HS, PsA and axSpA)
- Data from the Phase 3 VELA-TEEN trial may be combined with the Phase 3 VELA program in adults with moderate-to-severe HS to support the first Biologics License Application (BLA) for the Nanobody® sonelokimab

Zug, Switzerland, January 8, 2025 – MoonLake Immunotherapeutics (MoonLake; Nasdaq: MLTX), a clinical-stage biotechnology company focused on creating next-level therapies for inflammatory diseases, today announced that patients have been screened in three new trials across three new indications to evaluate sonelokimab, an investigational Nanobody® designed to treat inflammatory disease. The clinical program for sonelokimab now includes patients with adolescent hidradenitis suppurativa (HS), palmoplantar pustulosis (PPP) and axial spondyloarthritis (axSpA), in addition to adult patients with HS and active psoriatic arthritis (PsA). This increases the number of clinical trials led by MoonLake to ten and aligns with the plan to enroll over 3,000 patients in clinical trials with sonelokimab since the Company was founded in 2021.

Evidence indicates that activation of IL-17A and IL-17F plays a crucial role in the pathophysiology of these inflammatory diseases. Sonelokimab is designed to directly target sites of inflammation by inhibiting all relevant IL-17 dimers, namely the IL-17A/A, IL-17A/F, and IL-17F/F dimers, and to penetrate difficult-to-reach inflamed tissues. The initiation of the Phase 3 VELA-TEEN trial in HS, the Phase 2 LEDA trial in PPP and the Phase 2 S-OLARIS trial in axSpA expands the portfolio of sonelokimab to large dermatology and rheumatology indications, where significant unmet needs remain.

Dr. Jorge Santos da Silva, Founder and Chief Executive Officer of MoonLake Immunotherapeutics, said: "*The start of three new trials across three new dermatology and rheumatology indications underscores MoonLake's remarkable and rapid progress in independently realizing our ambitious plans. 2024 has been a year of execution, and 2025 is anticipated to mark a transformational and data-rich year as we look forward to notably reporting key Phase 3 data for HS, a market projected to reach $15bn by 2035. We are progressing towards registration and commercialization with a robust cash position. A huge thanks is due to our talented team for expanding possibilities, and of course, to all the patients and healthcare professionals for their participation in our trials.*"

Prof. Kristian Reich, Founder and Chief Scientific Officer at MoonLake commented: "*Building upon our ongoing Phase 3 studies in HS and PsA, we are further leveraging the molecular advantages of our Nanobody®, sonelokimab, in adolescent HS, PPP, and axSpA, all diseases characterized by activation of the IL-17 and IL-17F pathway in difficult-to-reach tissues. We are pioneering a paradigm shift in innovative trial design, which has given us the agility to rapidly execute these new clinical trials."*

Building upon the Phase 2 MIRA trial and ongoing Phase 3 VELA trials in adult HS, the Phase 2 ARGO trial and the ongoing Phase 3 IZAR trials in active PsA, the three new trials are:

Phase 3 VELA-TEEN: the first dedicated clinical trial in adolescent patients with moderate-to-severe hidradenitis suppurativa (HS)

- An open-label, single-arm trial with the primary endpoint to evaluate the pharmacokinetics, safety, and tolerability of the 120mg subcutaneous (SC) dose of sonelokimab over 24 weeks in 30-40 adolescents, aged 12-17, with moderate-to-severe HS, from U.S. sites with experience in pediatric dermatology.
- HS is a chronic, debilitating skin condition affecting an estimated 2% of the population. It often first manifests during adolescence, and adolescent patients are particularly physically and emotionally affected by the disease. Early intervention is therefore crucial to prevent disease progression and reduce the long-term physical and emotional impact.
    - Data from the VELA-TEEN trial may be combined with data from the Phase 3 VELA program in adults with moderate-to-severe HS to support a single Biologics License Application (BLA).
    - Topline data for the primary and secondary endpoints, including the higher clinical response level of HiSCR75, are anticipated in 2026.

Amy S. Paller, M.D, Walter J. Hamlin Professor and Chair of Dermatology and Professor of Pediatrics at Northwestern University Feinberg School of Medicine, and Principal Investigator of the trial commented: "*Adolescents with HS face substantial unmet medical needs and are a critically underserved patient population. The VELA-TEEN trial marks a significant advancement in HS treatment. By prioritizing early intervention, we hope to alter the disease course, reduce tissue destruction, and prevent permanent damage."*

Phase 2 LEDA: the first clinical trial in palmoplantar pustulosis (PPP) for an IL-17A and IL-17F inhibitor

- The trial aims to enroll approximately 30 patients across multiple sites to evaluate the 120mg SC dose of sonelokimab. The primary endpoint will be percent change from baseline in Palmoplantar Psoriasis Area and Severity Index (ppPASI) with important secondary endpoints including ppPASI75 (at least 75% improvement in the ppPASI).
- A biomarker-controlled clinical trial.
- The topline primary endpoint readout is expected during 2025.

Mark Lebwohl, MD, Dean for Clinical Therapeutics, Icahn School of Medicine at Mount Sinai, and Chairman Emeritus, Kimberly and Eric J. Waldman Department of Dermatology commented: *"Palmoplantar pustulosis is a chronic, recurrent inflammatory condition affecting the palms and soles, marked by aggressive pustule eruptions, skin destruction, and severe pain. This ongoing skin damage is debilitating, significantly impacting patients' daily lives and activities. Despite the severity, advanced therapies remain scarce. It is exciting to see studies with innovative technologies like nanobodies to address this urgent medical need."*

Phase 2 S-OLARIS: the first trial for an IL-17A and IL-17F inhibitor using an innovative design combining traditional clinical outcomes for axial spondyloarthritis (axSpA) with PET/MRI imaging

- An open-label trial to evaluate a 60mg SC dose of sonelokimab in approximately 25 patients with active axSpA. The primary endpoint is the change from baseline (CfB) at week 12 in the uptake of 18F-NaF in the sacroiliac joints and spine using PET in combination with MRI imaging. By combining established clinical measures with innovative PET imaging techniques and a biomarker program, the trial will for the first time measure sonelokimab's impact on deep tissue inflammation in unprecedented detail.
- axSpA is a chronic inflammatory condition that primarily affects the spine and sacroiliac joints, with a global prevalence ranging between 0.5% and 1.5%. Up to 40% of patients either do not respond to or cannot tolerate currently available treatments.
- The topline primary endpoint readout is expected in early 2026.

Professor Xenofon Baraliakos, Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Germany commented: *"Despite advancements in axial spondyloarthritis (axSpA) treatment over the past two decades, innovation remains crucial. Many patients experience inadequate responses to current therapies, and we need to continue to push the boundaries and explore novel approaches that can address not only inflammation across several domains but potentially modify the underlying disease processes. Integrating cutting-edge imaging techniques like MRI-PET with clinical outcomes, as being used in the S-OLARIS trial, offers a promising path forward. I am excited to see such a promising innovation like nanobodies, and specifically sonelokimab, being developed for axSpA. Our goal must be to develop more effective treatments that can improve long-term outcomes, reduce disease progression, and enhance the quality of life for all axSpA patients."*

The Company also plans to initiate a Phase 2 trial, P-OLARIS, in patients with active PsA using an innovative design combining traditional clinical outcomes with PET/MRI imaging.

- Ends -

About the VELA-TEEN trial
The Phase 3 VELA-TEEN trial is an open-label, single-arm trial designed to evaluate sonelokimab 120mg administered subcutaneously once every two weeks (Q2W) until week six and once every four weeks (Q4W) from week eight onwards. The trial aims to enroll 30-40 adolescents, aged 12-17, with moderate-to-severe hidradenitis suppurativa (HS), from U.S. sites experienced in clinical trials and pediatric dermatology. The primary trial phase will be 24 weeks with a primary endpoint evaluating the pharmacokinetics, safety, and tolerability of sonelokimab. VELA-TEEN will also evaluate several secondary endpoints, including the proportion of patients achieving the higher clinical response measure of the Hidradenitis Suppurativa Clinical Response Score (HiSCR) 75, in addition to HiSCR50. Other outcomes are the change from baseline in the International Hidradenitis Suppurativa Severity Score System (IHS4), which includes the quantitative measure of draining tunnels, and the proportion of patients achieving a meaningful reduction of the Children's Dermatology Life Quality Index (CDLQI) and the Patients Global Assessment of Skin Pain (PGA Skin Pain).

About Hidradenitis Suppurativa
HS 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 an estimated 2% of the 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 projected to reach $15bn 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-17F-mediated inflammation as a key driver of the pathogenesis of HS, with other identified risk factors including genetics, cigarette smoking, and obesity.

About the S-OLARIS trial
S-OLARIS is an open-label Phase 2 proof-of-concept trial aiming to investigate sonelokimab 60mg administered subcutaneously in approximately 25 patients with active axial spondylarthritis (axSpA). The primary endpoint is the change from baseline (CfB) at week 12 in the uptake of ^{18}F-NaF in the sacroiliac joints and spine using PET in combination with MRI imaging. Throughout the trial, several other endpoints will be assessed including established clinical disease activity outcomes (e.g., ASAS), scores related to physical function, spinal mobility, and enthesitis as well as patient reported outcomes. The trial also includes an exploratory peripheral blood and tissue biomarker program.

About active axial spondyloarthritis
AxSpA typically impacts young people, with diagnosis based on chronic inflammatory back pain lasting more than three months with onset under 45 years of age. Advanced disease can lead to progressive and pathologic bone formation and joint fusion, severely limiting spinal mobility. Global

reported prevalence of axSpA ranges from 0.5% to 1.5%. AxSpA can be categorized by disease progression into two subtypes: non-radiographic axSpA and ankylosing spondylitis (AS), also known as radiographic axSpA, which is diagnosed based on radiographic evidence of structural changes to the sacroiliac joints. Patients with axSpA experience fatigue, persistent morning stiffness, and pain that worsens at night and can disrupt sleep. Many patients also face the burden of comorbidities such as psoriatic arthritis and psoriasis. Studies have found elevated IL-17 levels in the blood and synovial fluid of patients with axSpA, and IL-17A and IL-17F are both thought to be key contributors to pathogenesis across the spondyloarthropathies.

About the LEDA Trial

The LEDA trial is a Phase 2 trial designed to evaluate the efficacy and safety of sonelokimab 120mg administered subcutaneously in adult patients with palmoplantar pustulosis (PPP). The primary endpoint of the trial is percent change from baseline in Palmoplantar Psoriasis Area and Severity Index (ppPASI) with important secondary endpoints including ppPASI75 (at least 75% improvement in the ppPASI). The LEDA trial features an innovative translational research program using peripheral blood and tissue biomarkers as trial controls.

The trial design has been informed by previous successful studies of sonelokimab, including the landmark Phase 2 MIRA trial in hidradenitis suppurativa, which identified the optimal dosing and demonstrated the potential of sonelokimab to target deep tissue inflammation effectively.

About Palmoplantar Pustulosis

PPP is characterized by the development of blister-like pustules within erythematous, scaly plaques on the palms and the soles of the feet. PPP typically develops in adulthood, more frequently impacts females. Patients frequently experience significant pain, burning, and itching sensations on the palms and soles of the feet which can be debilitating and impair their ability to work, sleep, or perform other activities of daily living. Currently, the treatment of PPP is challenging with a significant unmet need for novel therapies to reduce the symptom burden for patients. Evidence suggests that activation of the IL-17 pathway has an important role in disease pathophysiology.

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 psoriatic arthritis (PsA), and the Company is pursuing other indications in dermatology and rheumatology, including adolescent HS, PPP and axSpA.

For adults with 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.

A Phase 3 trial, VELA-TEEN, is also ongoing in adolescent HS, a disease that typically begins at this early stage of a patient's life, and is also the period in which irreversible damage and inflammatory remission are most critical.

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 approximately 60% 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 an 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.

Sonelokimab is also being assessed in the Phase 2 LEDA trial, which is ongoing for palmo-plantar pustulosis (PPP), a debilitating inflammatory skin condition affecting a significant number of patients.

Additionally, Sonelokimab is being assessed in the ongoing Phase 2 S-OLARIS trial, for active axSpA. The trial features an innovative design complementing traditional clinical outcomes with cellular imaging techniques.

Sonelokimab has also been assessed in a randomized, placebo-controlled third-party 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 third-party 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.

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 IL-17F/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 timing of topline results of the Phase 3 VELA-TEEN clinical trial of sonelokimab in adolescent patients with HS, Phase 2 LEDA clinical trial of sonelokimab in patients with PPP, Phase 2 S-OLARIS trial in patients with axSpA, Phase 3 VELA trials in adult HS and Phase 3 IZAR trials in active PsA and initiation of Phase 2 P-OLARIS trial in patients with active PsA, the efficacy and safety of sonelokimab for the treatment of adult HS, adolescent HS, PPP, PsA and axSpA, including in comparison to existing standards or care or other competing therapies, clinical trials and research and development programs, including the combination of data from the VELA-TEEN trial in adolescents with data from the Phase 3 VELA program in adults with moderate to severe HS to support a single BLA, the anticipated timing of the results from those studies and trials and potential market opportunities for sonelokimab and MoonLake's anticipated cash position. 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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