MoonLake Immunotherapeutics announces publication in The Lancet

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MoonLake Immunotherapeutics announces publication in The Lancet of impressive Phase 2b data showing its Tri-specific Nanobody® Sonelokimab totally clears skin in almost 6 out of 10 patients with moderate to severe psoriasis

- Sonelokimab showed significant clinical benefit with rapid onset and a good safety profile, with clear skin (PASI 100) achieved in up to 57% of patients at Week 24 and sustained responses over 52 weeks
- First Phase 2 evaluation of a Nanobody® IL-17A/F inhibitor in psoriasis included secukinumab, an IL-17A inhibitor, as active control
- Unique, small size Nanobody® Sonelokimab provides balanced inhibition of IL-17A and IL-17F and has an albumin binding site which may enable deep tissue penetration in skin and joints
- MoonLake plans to accelerate Sonelokimab's development program in inflammatory diseases driven by IL-17A and F, like psoriatic arthritis, ankylosing spondylitis, hidradenitis suppurativa and psoriasis

ZUG, Switzerland, May 6, 2021 – MoonLake Immunotherapeutics AG, a clinical-stage biotechnology company focused on creating next-level therapies for inflammatory skin and joint diseases, today announced that full results of a Phase 2b study of its Tri-specific Nanobody® Sonelokimab were published in The Lancet[7]. Sonelokimab is an investigational IL-17A/IL-17F inhibitor with an albumin binding site, which has the potential to facilitate deep tissue penetration in the skin and joints[1]. It has clinically demonstrated potential to allow better disease control in dermatology and rheumatology patients. Sonelokimab showed impressive efficacy with a favorable safety profile, and numerically outperformed active control secukinumab.

In the study, dosages up to 120 mg showed rapid and significant clinical benefit compared with placebo. In the highest dosage group, almost 6 out of 10 patients (57%) achieved total skin clearance (PASI 100 response) after 24 weeks. Rapid response was demonstrated with one of three patients already achieving almost clear skin (PASI 90 response) by week 4. Analysis of an individualized dosing scheme including off-drug periods in controlled patients revealed durable responses over one year. Sonelokimab was generally well tolerated, with a safety profile similar to the active control, secukinumab, and an overall candida rate of 7.4%. Although the highest dosage and schedule could be used for future clinical studies, additional assessment and modelling may aid in the final selection of the optimal dosage and schedule. The trial was conducted by Avillion LLP under a 2017 co-development agreement with Merck KGaA, Darmstadt, Germany.

Investigator Kristian Reich MD, PhD, Chief Scientific Officer and co-founder of MoonLake Immunotherapeutics, commented: "*Sonelokimab is a remarkable Nanobody with game-changing potential in the treatment of a range of IL-17A/F-driven inflammatory diseases. This study shows very high response levels in the model disease psoriasis, with a favorable benefit-safety profile. MoonLake's aim is to also accelerate Sonelokimab's development in other inflammatory diseases driven by IL-17A and IL-17F like psoriatic arthritis, ankylosing spondylitis and hidradenitis suppurativa. Our aim is to elevate treatment goals in these diseases based on the unique characteristics of Sonelokimab, giving patients with common and burdensome skin and joint conditions a chance of better disease control.*"

Mark Weinberg, MD, MBA, co-author of the publication and Chief Medical Officer of Avillion LLP, commented: *"Following completion of our Phase 2b activities with Merck KGaA, we are excited to see Solenokimab continue in development. Data on this Tri-specific Nanobody demonstrates potential in major inflammatory diseases driven by IL-17A and IL-17F. These diseases have a profound effect on patients' lives not just physically but emotionally and socially. We've seen a continued evolution of biologic therapies in the last 25 years and I am looking forward to seeing further development of this novel nanobody biologic by MoonLake."*

The randomized, double-blind, placebo controlled, multi-center, Phase 2b study was designed to assess efficacy, safety and tolerability of Sonelokimab in subjects with moderate-to-severe chronic plaque-type psoriasis. The trial enrolled 313 patients (age 18-75) with chronic plaque psoriasis for at least six months, with an Investigator Global Assessment (IGA) score ≥3, involved body surface area ≥10%, and Psoriasis and Severity Index (PASI) ≥12 at screening and at baseline. Patients were randomized to one of four dose regimens of Sonelokimab, or a placebo comparator arm, or a reference arm (secukinumab).

This clinical trial significantly expands the number of patients and duration of therapy evaluated for Sonelokimab in plaque psoriasis and represents the first Phase 2 evaluation of a Nanobody® IL-17 A/F inhibitor in psoriasis. The study found Sonelokimab was efficacious in the treatment of plaque psoriasis. The safety profile reflects the mechanism of action with oral Candida as the most reported adverse event, in the same range as IL-17A inhibitors (7.4%).

MoonLake Immunotherapeutics was established by an international team of immunology specialists to accelerate the clinical development of Sonelokimab, building on robust clinical data generated by Merck KGaA, Darmstadt, Germany, and by Ablynx, a Sanofi company, which discovered the molecule.

MoonLake Immunotherapeutics plans to accelerate the development of Sonelokimab in multiple inflammatory diseases in dermatology and rheumatology driven by IL-17A and IL-17F. This group of IL-17A/F Inflammatory Diseases (introducing the novel concept of AFID) includes psoriatic arthritis, ankylosing spondylitis, and hidradenitis suppurativa – conditions affecting millions of people worldwide with a large need for improved treatment options. MoonLake Immunotherapeutics plans to initiate multiple Phase 2 trials soon.

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Notes to Editors

About Sonelokimab

Sonelokimab is a Tri-specific IL-17A/F Nanobody® with the potential to be best-in-class across several indications. It specifically targets IL-17A and IL-17F in a balanced way, and it has an albumin binding site, which together with the small size of the Nanobody® may facilitate deep skin and joint penetration and an extended half-life[2]. Deep tissue penetration potentially allows for better efficacy in difficult-to-reach tissues like joints, nails, scalp and deep skin. The extended half-life allows for convenient once-a-month subcutaneous dosing. The inhibitory profile of Sonelokimab is balanced, and as a consequence may have the combination of best-in-class efficacy in AFIDs with an optimized benefit-risk profile.

About AFID (IL-17A/F Inflammatory Diseases)

AFID is a novel concept aiming to classify inflammatory diseases in which over-expression of the cytokines IL-17A and IL-17F is a major driver of the pathophysiology. Millions of people are suffering from AFIDs and there are limited treatment options for high-level clinical improvement. AFIDs include:

- Psoriatic arthritis (PsA) (prevalence: ~0.65%); ~40% of patients living with PsA have axial disease[3,4]
- Axial spondylo-arthritis (AS) (prevalence: 0.5 - 1.4%); split into non-radiographic axial SpA (nr-axSpA) and ankylosing spondylitis (r-axSpa, prevalence: ~0.3%)[5]
- Hidradenitis suppurativa (HS) (prevalence: ~0.7-1.2%); currently underdiagnosed/undertreated with limited effective treatment options available[5]
- Psoriasis (prevalence: ~2.5%); more than 1/3 of patients living with psoriasis have psoriatic arthritis or other persistent manifestations, such as nail disease[2]
- Other potential AFIDs include palmoplantar pustulosis (PPP), generalized pustular psoriasis (GPP) and pyoderma gangrenosum (PG)

About Nanobodies® (single-domain antibodies)

A single-domain antibody (sdAb), also known as a Nanobody®, is an antibody fragment consisting of a single monomeric variable antibody domain. Like antibodies, Nanobodies® are able to bind selectively to a specific antigen with high affinity.

Whole antibodies are composed of two immunoglobulin heavy chains and two light chains. The first single-domain antibodies were engineered from heavy-chain only antibodies to create an antibody fragment – a Nanobody®. Nanobodies® have the same or higher affinity and specificity compared to traditional antibodies yet have approximately 1/10th of the molecular weight. They offer a number of potential advantages including an easier manufacturing process, a higher thermostability, and the potential to create multivalent molecules with enhanced ability to penetrate inflamed tissue, especially when containing an additional albumin binding domain such as Sonelokimab[1]. The terms Nanobody® and Nanobodies® are trademarks of Ablynx, a Sanofi company.

About MoonLake Immunotherapeutics

MoonLake Immunotherapeutics AG, founded in 2021, is a clinical-stage biopharmaceutical company leveraging Nanobody® technology to develop next-level medicines for immunologic diseases, including inflammatory skin and joint diseases. MoonLake Immunotherapeutics has a portfolio of therapeutic programs based on Sonelokimab (M1095/ALX-0761), a biologic molecule potentially capable of driving disease modification in dermatology and rheumatology patients.

1) Papp KA et al. Lancet 2021; 397:1564-75

2) Coppegieters K et al., Arthritis Rheum 2006; 54:1856-66; Tijink BM, et al. Mol Cancer Ther. 2008;7:2288-97

3) Reich K, et al. Br J Dermatol. 2009; 160:1040-1047

4) Alinaghi F, et al. J Am Acad Dermatol. 2019; 80:251-265.

5) Dean LE et al. Rheumatology 2014; 53:650–657.

6) Nguyen TV, et al. J Eur Acad Dermatol Venereol. 2021; 35:50-61.

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