AMYRA Successfully Demonstrates a New Therapeutic Paradigm for Gluten-Related Disorders in a First-in-Human Study

- *Lead product AMYNOPEP achieves proof-of-principle in exploratory clinical study*
- *AMYNOPEP is the first and only gluten-digesting enzyme combination that supports and enhances the activity of critical enzymes on the lining of the intestinal brush border*

Basel (Switzerland), October 23, 2024 – AMYRA Biotech AG ("AMYRA"), a company developing novel, oral digestive enzyme therapeutics for gastrointestinal diseases announced the peer-reviewed publication of its clinical proof-of-principle study with its lead product AMYNOPEP in *Frontiers in Immunology – Nutritional Immunology* (https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2024.1425982/full). AMYNOPEP is the first and only gluten-digesting enzyme combination that supports and enhances the activity of critical endogenous enzymes on the lining of the small intestine. AMYNOPEP is designed to break down hard-to-digest gluten peptides into harmless and absorbable single amino acids and dipeptides, thereby supporting individuals with gluten-related health disorders in avoiding exposure to inflammatory peptides. AMYRA's first-in-human clinical study assessed gluten-digesting enzyme efficacy using high-resolution analytics and demonstrated in near-real-time that AMYNOPEP swiftly and significantly enhanced the digestion of proteolytically-resistant, immunogenic gluten peptides in healthy volunteers.

A team of researchers from AMYRA and the University of Greifswald (Germany) evaluated AMYNOPEP's digestive efficacy on the degradation of a long, proteolytically resistant gluten peptide known as the 33-mer, which has been associated with an adverse immune response in celiac disease. The digestion efficacy of AMYNOPEP on the 33-mer was first assessed *in vitro*, demonstrating end-to-end degradation of the gluten immunogenic peptide into single amino acids and dipeptides. These *in vitro* results were then validated in a crossover study of 14 healthy volunteers who received stable isotope-labelled 33-mer with and without AMYNOPEP. The study clearly showed that AMYNOPEP enhanced 33-mer digestion kinetics within minutes, significantly increasing levels of stable isotope-labelled amino acids detected in blood. Strikingly, AMYNOPEP improved 33-mer digestion even under "stress-test" conditions that included competing food substrates such as hydrolyzed whey protein and wheat gluten, revealing up to 3 times higher maximum concentrations of labelled amino acids in blood with AMYNOPEP compared to control.

"The positive results of this proof-of-principle study pave the way for a new therapeutic enzyme paradigm leveraging specific exopeptidase combinations that support, enhance, or even replace the activity of critical endogenous enzymes lining the small intestine," said Dr. Sulay Mourabit, CSO of AMYRA and co-lead author on the study. In the human gastrointestinal tract, most exopeptidases are found at the intestinal brush border membrane, which is sensitive to inflammatory damage. These exopeptidases are essential for completing protein digestion by cleaving peptides from end-to-end, generating absorbable amino acids. He added: "As single agents, exopeptidases are inefficient as they have limited substrate range, and we see this with DPP-IV supplements currently on the market. AMYRA specializes in developing unique combinations of exopeptidases with complementary and enhanced activity, designed to thoroughly break down proteolytically resistant food peptides. Ultimately, complex digestive diseases such as celiac may require a combination of treatment approaches. Given the critical

role of the exopeptidase machinery in the human GI tract, and the vulnerability of the intestinal brush border membrane to chronic inflammatory damage, we're excited to see the role that AMYNOPEP will play in digestive disease therapeutics."

"This is an encouraging and far-reaching proof-of-principle study demonstrating the validity and therapeutic relevance of our approach," said Dr. Werner Tschollar, CEO and founder of AMYRA and senior author of the study. "As a next step, AMYRA is planning further clinical studies to investigate AMYNOPEP's enzyme efficacy, immune response suppression, and symptom relief in patients with celiac disease. We strongly believe that supplementing the body with specific exopeptidases will prove to be a valuable adjunct therapy to the gluten-free diet, which alone represents a suboptimal solution."

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About AMYRA Biotech AG
AMYRA Biotech AG is a privately held biotech company developing novel therapeutic solutions for patients suffering from dietary peptide-driven disorders including celiac disease, gluten sensitivity, and other gastrointestinal disorders. The Company's proprietary enzyme combinations have the unique capability of rapidly and systematically digesting proteolytically resistant gluten peptides from one end to the other, generating harmless and absorbable degradation products in the small intestine. AMYRA is based in Basel, Switzerland. For further information, please visit www.amyra.com.

About AMYNOPEP
Several digestive enzyme supplements on the market and therapeutics under development seek to help the body break down hard-to-digest gluten peptides, which are known to trigger adverse reactions in individuals with gluten-related health disorders. The vast majority of these are endopeptidases that target gluten digestion in the stomach and generate smaller protein fragments (peptides) that may retain the ability to trigger an inflammatory response. In contrast, AMYNOPEP is a novel therapeutic enzyme principle based on specific combinations of exopeptidases that thoroughly degrade gluten peptides from end-to-end in the small intestine, generating individual, easily absorbable, and harmless amino acids and dipeptides that are incapable of triggering an immune response. AMYRA's lead exopeptidase combination, AMYNOPEP, is capable of digesting proline-rich, hard-to-digest peptides found in foods such as gluten, which is notoriously linked to gastrointestinal distress.

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