adimune™

TRANSFORMING AUTOIMMUNE DISEASE TREATMENT THROUGH RESTORED IMMUNE TOLERANCE

ADI-100: a ground-breaking approach to autoimmune disorders

An aditXt company (Nasdaq: ADTX)

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MISSION & LEADERSHIP

“ Our mission is to address the root causes of autoimmune diseases. By harnessing the body’s natural ability to restore immune tolerance, we strive to deliver innovative solutions that improve lives without the risks of immunosuppression.”

Dr. med. Joachim-Friedrich Kapp

Co-CEO, Adimune

- 30+ years in global pharma leadership.
- Former President, Therapeutics at Schering AG.
- Expertise in immune modulation and clinical innovation.

Amro Albanna

Co-CEO, Adimune

- 25+ years of leadership in innovation and entrepreneurship.
- Founded and led eight startups across health and tech sectors.
- Expertise in driving commercialization, M&A, and IPOs.

AUTOIMMUNE DISEASES REPRESENT A LARGE, YET STILL UNDER-SERVED MARKET

TAM $84.12 B

Autoimmune diseases affect 8% of people in the U.S., with prevalence increasing YoY

*National Institutes of Health (NIH) Autoimmune Diseases Coordinating Committee. Progress in Autoimmune Diseases Research (Publication No. 05–5140). March 2005. 14, Accessed date: October 25, 2022;

- **Type 1 Diabetes:** Affects approximately 9 million people globally, with the incidence rising by 3-4% annually, particularly among children. Current treatment depends heavily on insulin therapy, which does not address the underlying autoimmune process.
- **Psoriasis:** Impacts over 125 million individuals worldwide, causing chronic inflammation and severe quality-of-life impairments. Many patients remain unresponsive, experience adverse effects or diminishing efficacy from existing therapies.
- **GAD-antibody disorders of the CNS:** various neurological autoimmune diseases including Stiff-Person Syndrome.

* World Health Organization. (n.d.). *Diabetes.* Retrieved December 6, 2024, from https://www.who.int/news-room/fact-sheets/detail/diabetes

* National Psoriasis Foundation. (n.d.). *Psoriasis statistics.* Retrieved December 6,2024 from https://www.psoriasis.org/psoriasis-statistics/

THE DECISION MAKING OF THE MOUSE IMMUNE SYSTEM IN THE PRESENCE OF A DYING CELL

Is a cell dying because of infection/damage/ disease or normal turnover?

- In case of infection, damage or disease, the immune system activates its aggressive instruments (Steinman et al. 2000)
- In case of normal turnover, the immune system signals tolerance to the antigens presented (Steinman et al. 2000)

The Aditxt approach

- ADI-100 is designed to induce a small number of dying cells locally to mimic normal turnover (Li et al. 2010)
- ADI-100 then presents the antigen msGAD55, a modified form of the antigen GAD65, which is the target of autoimmune attack. (Li et al. 2010)

How ADI-100 exerts its activity with the immune system

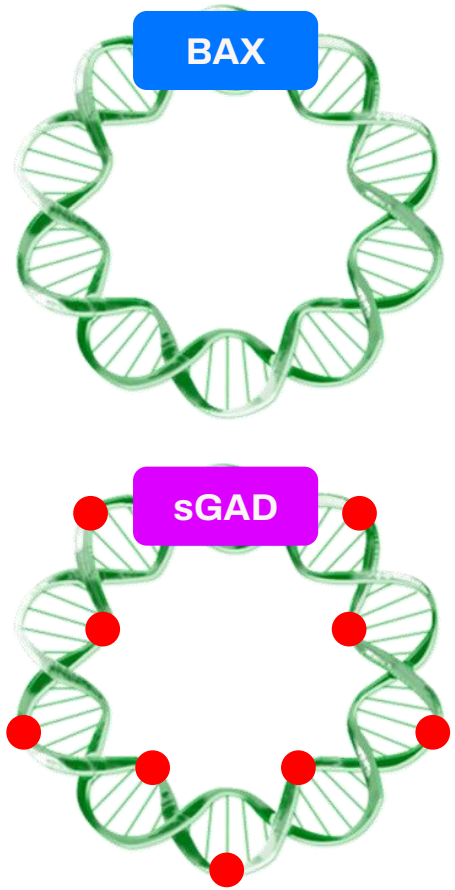
- The immune system takes up the antigen msGAD55, activates the tolerizing system and scans for related antigens, e.g. GAD65 and others which are maintaining the autoimmune process (Li et al. 2010)
- ADI-100 is designed to downregulate the antibodies against GAD65, which contribute to the autoimmune disease and block the production of GABA.
- Restored GABA levels allow its inhibitory function, adding to the tolerization process. (Bhat et al. 2010)

Studies have not been conducted in humans

MECHANISM OF ACTION (mouse data)

How ADI-100 Works: (Li et al. 2010; Alleva et al. 2020)

- **Precision Immune Reprogramming**: Retrains the immune system to recognize "self" through apoptotic signalling and antigen presentation, restoring immune tolerance - implied restored GABA-inhibitory function. **Dual DNA Mechanism**:
    - **Pro-Apoptotic DNA Molecule (BAX)**: Local in-vivo induction of programmed cell death to initiate the tolerization process.
    - **Methylated Antigen DNA Molecule (GAD)**: Encodes the secreted form of a dominant antigen to mimic natural processes, retrain the immune system, and restore immunological balance.
- **Antigen-Specific Tolerance**: Targets auto-immune reaction against glutamic acid decarboxylase (GAD65), a key driver in Type 1 Diabetes, Psoriasis, and certain CNS autoimmune disorders.
- **Bystander Effect:** Modulates immune responses by including a broader spectrum of antigens involved in the pathogenesis, expanding therapeutic applications to related autoimmune skin and CNS conditions and prevention of type 1 diabetes.



Studies have not been conducted in humans

THE RELEVANCE OF GAD AND GABA IN AUTOIMMUNE DISEASES (Dade et al. 2020)

- The mechanism of action of ADI-100 implies restoring **GABA** levels in the immune system, the pancreas, in skin and the CNS. (not proven in humans)
- Glutamic Acid Decarboxylase (GAD) is the rate-limiting enzyme for the synthesis of the inhibitory gamma-aminobutyric acid (GABA).
- Anti-GAD antibodies inhibit the function of the enzyme thereby reducing GABA levels.
- Although the underlying mechanisms have not been fully elucidated yet, it has been extensively demonstrated that GAD autoimmunity interferes with the GABA-inhibitory function.
- Conclusion: Downregulation of anti-GAD antibodies by ADI-100 leads to GABA regaining its inhibitory function adding to the tolerizing process.

CURRENT STATUS

Focus: With its drug candidate ADI-100, Adimune is focused on restoring immune tolerance.

Innovative Technology: Extensive IP Portfolio: Over **152 issued and pending patents**, protecting and enhancing Adimune's innovation portfolio.

Preclinical Validation: Restoring Immune Tolerance

Type 1 Diabetes:

Reversed hyperglycaemia and restored functional islet cell mass in NOD mouse models; counteracted Checkpoint-Inhibitor-enhanced type 1 diabetes in NOD mice without interfering with the anti-tumour effect of the Checkpoint Inhibitor.

Psoriasis:

Efficacy demonstrated through downregulation of pro-inflammatory activity in the Imiquimod (IMQ) psoriasis model.

Comprehensive animal Safety Studies:

- GLP preclinical toxicology data confirm no significant adverse effects, no persistence in organ tissues, and no formation of anti-plasmid antibodies.

Regulatory Milestones:

- Stability studies remain to be completed
- Clinical Trial Application is expected to be filed for Psoriasis and Type1 Diabetes in Germany. IND submission is planned for the study at Mayo Clinic.

SAFETY: A SUMMARY OF ADI-100 PRECLINICAL TOXICOLOGY STUDY

Study Design:

- Weekly intradermal administration of 50 µg and 100 µg BAX+msGAD (ADI-100) for nine weeks to evaluate safety, tolerability, and biological impact.

Key Findings:

- No premature deaths or signs of local intolerance.
- No adverse effects were observed on clinical parameters, including body weight, weight gain, food consumption, biochemistry, and urinalysis.
- No evidence of anti-nuclear antibody production, no significant macroscopic post-mortem findings, and no histopathological abnormalities.

Haematological Observations:

- Administration of 100 µg resulted in a significant reduction in neutrophilic and eosinophilic granulocyte counts. These changes did not revert to baseline by the end of the three-week recovery period. No impact on platelet counts was noted.

Immunogenicity and Persistence:

- No formation of anti-plasmid antibodies, ensuring immunological safety.
- No persistence of the drug product in organ tissues, underscoring its transient and controlled mechanism of action.

ADIMUNE'S VISION FOR AUTOIMMUNE DISEASE TRANSFORMATION

Type 1 Diabetes

- **Treatment:** In preclinical studies, ADI-100 demonstrated durable (>300 days) efficacy in type 1 diabetes models with no impact on general immune responsiveness to infections or tumor growth. The protective immune modulation observed in animal models was successfully transferable to a new cohort of animals (adoptive transfer).
- **Prevention:** ADI-100 is designed to target the early immune mechanisms responsible for beta-cell destruction in the pancreas, aiming to pre-empt disease onset in high-risk individuals. This prevention strategy leverages the downregulation of aggressive immune activity to maintain pancreatic beta cell function.

Autoimmune Skin and CNS Disorders

- **Potentially Broad Application:** ADI-100 facilitates the downregulation of pathogenic immune responses, designed to present a transformative approach for treating autoimmune skin diseases, such as psoriasis, and anti-GAD-mediated CNS disorders, including Stiff-Person Syndrome.

THE RELEVANCE OF THE BYSTANDER EFFECT FOR FUTURE DEVELOPMENT PLANS

- **Endocrinology:** Upon demonstrating efficacy in Type 1 Diabetes and the successful downregulation of anti-GAD antibodies, ADI-100 will be poised for subsequent prevention studies targeting early disease stages in at-risk populations.
- **Dermatology:** If ADI-100 proves effective in psoriasis, its application may expand to encompass other autoimmune skin disorders, providing a versatile platform for dermatological innovation.
- **Neurology:** If efficacy can be established in Stiff-Person Syndrome, ADI-100's mechanism of action could address a large spectrum of CNS autoimmune diseases driven by anti-GAD immunity, unlocking new therapeutic possibilities.

CLINICAL PROGRAM

Program in the United States

Partnered with the Mayo Clinic to initiate an investigator-sponsored study targeting Stiff-Person Syndrome.

MAYO CLINIC

Program in Europe

Received supportive Scientific advice from the Paul-Ehrlich-Institute (March 2023), laying the groundwork for regulatory submissions.

Clinical trial applications in Germany to initiate mono-national studies:

- Psoriasis: Targeting chronic autoimmune-driven skin inflammation.
- Type 1 Diabetes: Focusing on halting autoimmune destruction of pancreatic beta cells.

Paul-Ehrlich-Institut

Preclinical Research Expansion

Allergy models planned at the renowned Helmholtz Institute in Munich to evaluate ADI-100's broader applicability in immunological disorders.

HELMHOLTZ MUNICH

COMMERCIALIZATION STRATEGY

Monetization Opportunities:

- Licensing, co-development partnerships, or product sales to pharmaceutical and biotech partners.
- Focused on leveraging Adimune's proprietary ADI-100™ platform for early-stage collaboration opportunities and downstream revenue potential.

Comparative Benchmarks:

- **Three recent deals between biotech companies and pharma partners**:
  - Two separate deals focused on immune tolerance and immune modulation technologies. Secured early-stage co-development agreements with major pharmaceutical companies, achieving total deal values of $500M–$1B.
  - December 3rd., 2024, a deal between a major pharma company with a biotech firm in the autoimmune field potentially worth more than $900M

Future Outlook:

- Targeting high-value licensing and co-development deals to drive early revenue streams.
- Strategic positioning for acquisition or spinoff following Phase II clinical trial success.

Adimune's USPs:

- **Ground-Breaking Mechanism:**
  ADI-100™ leverages a unique, biologically inspired approach to immune tolerance, mimicking the body's natural ability to regulate immune responses. This makes it an attractive and differentiated candidate for licensing and co-development deals.
- **Broad Market Applications:**
  Designed to address significant unmet needs in severe but also in mild to moderate Psoriasis, Type 1 Diabetes, and CNS autoimmune disorders, targeting markets with multi-billion-dollar growth potential.
- **Scalability and Flexibility:**
  ADI-100™'s versatile platform offers opportunities for expansion into adjacent autoimmune and inflammatory disease indications, making it a valuable asset for long-term partnerships and strategic acquisitions.

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THANK YOU

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