DIAMYD MEDICAL

Diamyd® for the Treatment of Autoimmune Diabetes

Stockholm NASDAQ First North Growth Market – DMYD B

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Diamyd®: Revolutionizing Type 1 Diabetes Treatment with Antigen-Specific Immunotherapy

Diamyd®, an innovative **antigen-specific immunotherapy** targeting a large genetic subgroup of **Type 1 Diabetes** (T1D), is the only disease-modifying treatment in T1D in late-stage development

Currently in **pivotal Phase 3** across Europe and the US, Diamyd® is designed to **preserve beta cell function**

With **Fast Track** and **Orphan designations**, as well as support for an **Accelerated Approval pathway** by the **FDA**, Diamyd® is poised for a **potential BLA 2026**

Supported by US payers, with a pricing model around **$200,000 per treatment**, Diamyd® has a first addressable market worth over **$5 billion in the US alone**

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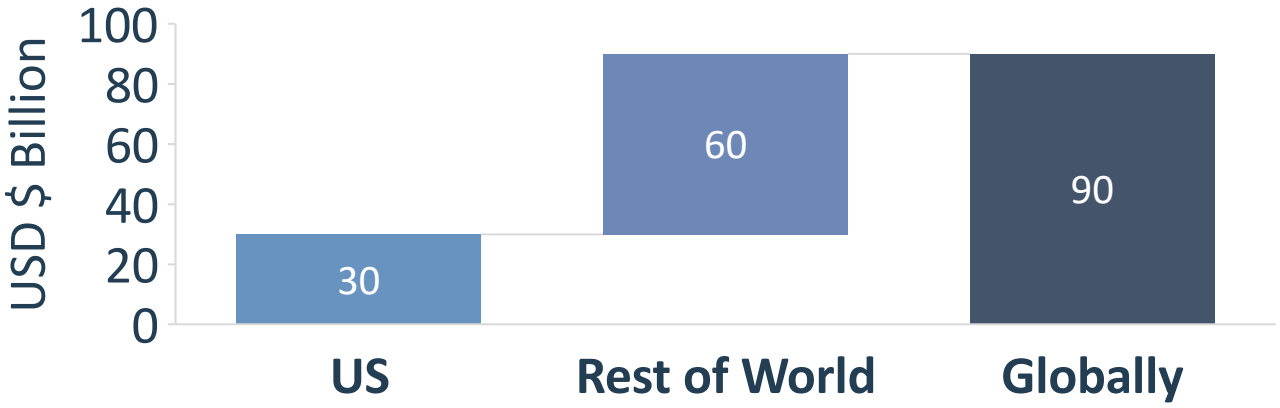
Autoimmune Diabetes: Unmet need & economic burden

Type 1 Diabetes (T1D)

~ 500,000 new cases every year

- More common in Western countries, especially Scandinavia
- Life-long dependence on insulin therapy and blood glucose monitoring

>$90 BN global annual economic burden*



Latent Autoimmune Diabetes in Adults (LADA)

>2 million new cases every year

- 10% of all Type 2 Diabetes patients may have autoimmune diabetes with GAD autoantibodies and faster progression to insulin dependence
- Common in Western countries, but also in India, China and Japan

*Modelling the total economic value of novel T1D therapeutic concepts, January 2020, Health Advances.

High risk of serious complications, shorter life-expectancy, decreased quality of life and significant health economic costs

Disease modifying therapies for T1D are predicted to have a multibillion-dollar economic impact - in the US alone

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Accelerating interest for autoimmune diabetes from pharma & regulators

Mar 2023	**$2.9 billion** acquisition of **Provention Bio** by **Sanofi**. **FDA-approved** immunotherapy **TZIELD** to delay onset of T1D. Sanofi leading concerted effort to raise T1D awareness and build the screening and treatment infrastructure for disease-mofifying therapies.
2019-2023	**Vertex Pharmaceuticals** acquired **Semma Therapeutics** in 2019 ($950M) and **ViaCyte** in 2022 ($320M); **CRISPR Therapeutics** $100M upfront licensing deal in 2023
Apr 2023	**Novo Nordisk** partnership with **Aspect Biosystems** ($75M upfront and milestones up to $650M) to produce 3D printed cells
Jun 2023	**FDA** approved **cell therapy Lantidra** for treatment of difficult-to-control adult T1D
Jun 2023	Eli Lilly acquired cell therapy company **Sigilon** in 2023 (deal worth up to $500M)

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Clinical Pipeline

Diamyd® is the only disease-modifying therapy in the world for T1D in Phase 3 development

PROGRAM		DEVELOPMENT				STATUS	
Study / Indication	Asset	Preclinical	Phase 1	Phase 2	Phase 3	Global Rights	Milestones
DIAGNODE-3 Recent-onset Stage 3 T1D with HLA DR3-DQ2 & GADA	**Diamyd®**	**Fast track designation, Orphan designation, R&D partnership with Breakthrough T1D**				DIAMYD MEDICAL	**Ongoing** in EU & US, early readout ~March 2026
DiaPrecise Stage 1 & 2 T1D with HLA DR3-DQ2 & GADA	**Diamyd®**					DIAMYD MEDICAL	**Started** Q4 2023
DIAGNODE-B T1D with HLA DR3-DQ2 & GADA; 4th or 5th ”booster” dose	**Diamyd®**					DIAMYD MEDICAL	**Completed**, topline results announced Q4 2023
GADinLADA LADA with HLA DR3-DQ2 & GADA	**Diamyd®**					DIAMYD MEDICAL	**Completed**, topline presented at EASD 2022, published
RegGenerate-1 T1D for more than 5 years	**Remygen®**					DIAMYD MEDICAL	**Completed**, topline announced Q2 2023
Insulin-based antigen-specific therapy to treat and prevent T1D with HLA DR4-DQ8 and IAA							

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Diamyd®

Recombinant GAD65 Formulated in Alum (rhGAD65/alum)

Primary Indication (Fast Track and Orphan designation)
Type 1 Diabetes (stage 3) with residual beta cell function and HLA type DR3-DQ2

Label Expansion
Type 1 Diabetes prevention (stage 1 & 2), Fast Track designation
LADA

Mechanism of Action
Induce immunological tolerance against GAD65

Clinical Effect and Benefit
Preserve the endogenous insulin production, reduce short- and long-term complications

Mode of Administration
Three intranodal injections one month apart

Development Status
Phase III – Stage 3 T1D
Phase I/II – Stage 1&2 T1D
Phase I/II - LADA

Licensing Status
Global rights available

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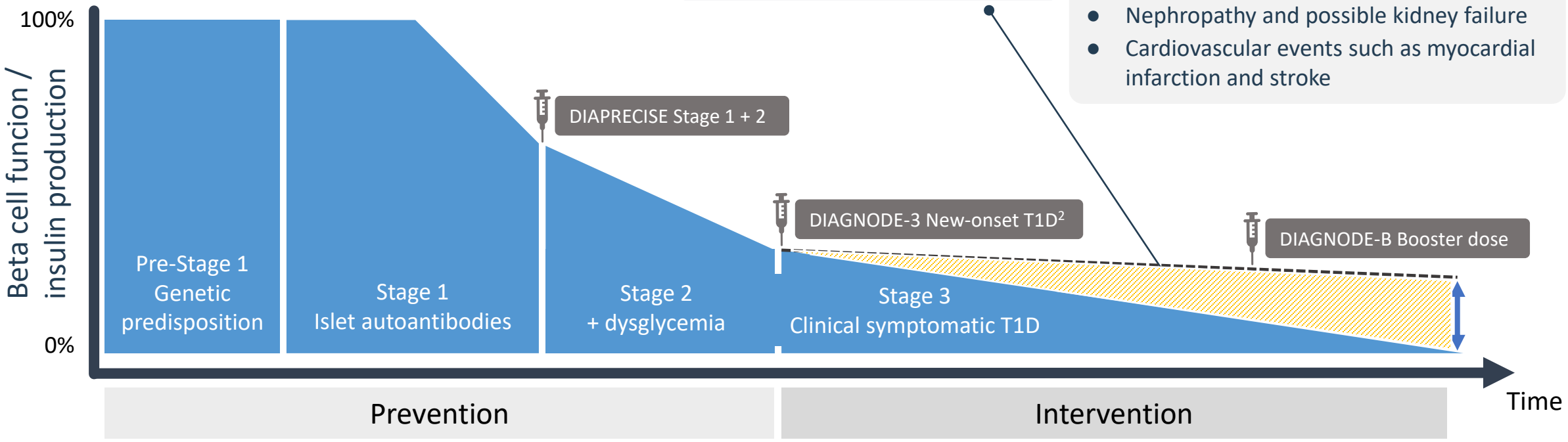
Focus on preemptive medicine

Diamyd® is designed to prevent diabetes complications and improve glucose control by stopping the autoimmune destruction of beta cells

Illustrative decline of functional beta cell mass in autoimmune diabetes



Reduced risk of[1]

- Severe hypoglycemia
- Life-threatening ketoacidosis
- Retinopathy and possible blindness
- Neuropathy and possible limb amputation
- Nephropathy and possible kidney failure
- Cardiovascular events such as myocardial infarction and stroke

[1] Lam et al. J Clin Invest. 2021 Feb 1;131(3):e143683. Gubitosi-Klug et al. J Clin Invest. 2021;131(3):e143011. McGee et al. Diabet Med. 2014;31(10):1264–1268. doi: 10.1111/dme.12504. Steffes et al. Diabetes Care. 2003;26(3):832–836. Palmer et al. Diabetes. 2004;53(1):250–264.DCCT Investigators. Ann Intern Med. 1998;128(7):517–23.

[2] Within 6 months from clinical diagnosis of (Stage 3) clinical T1D

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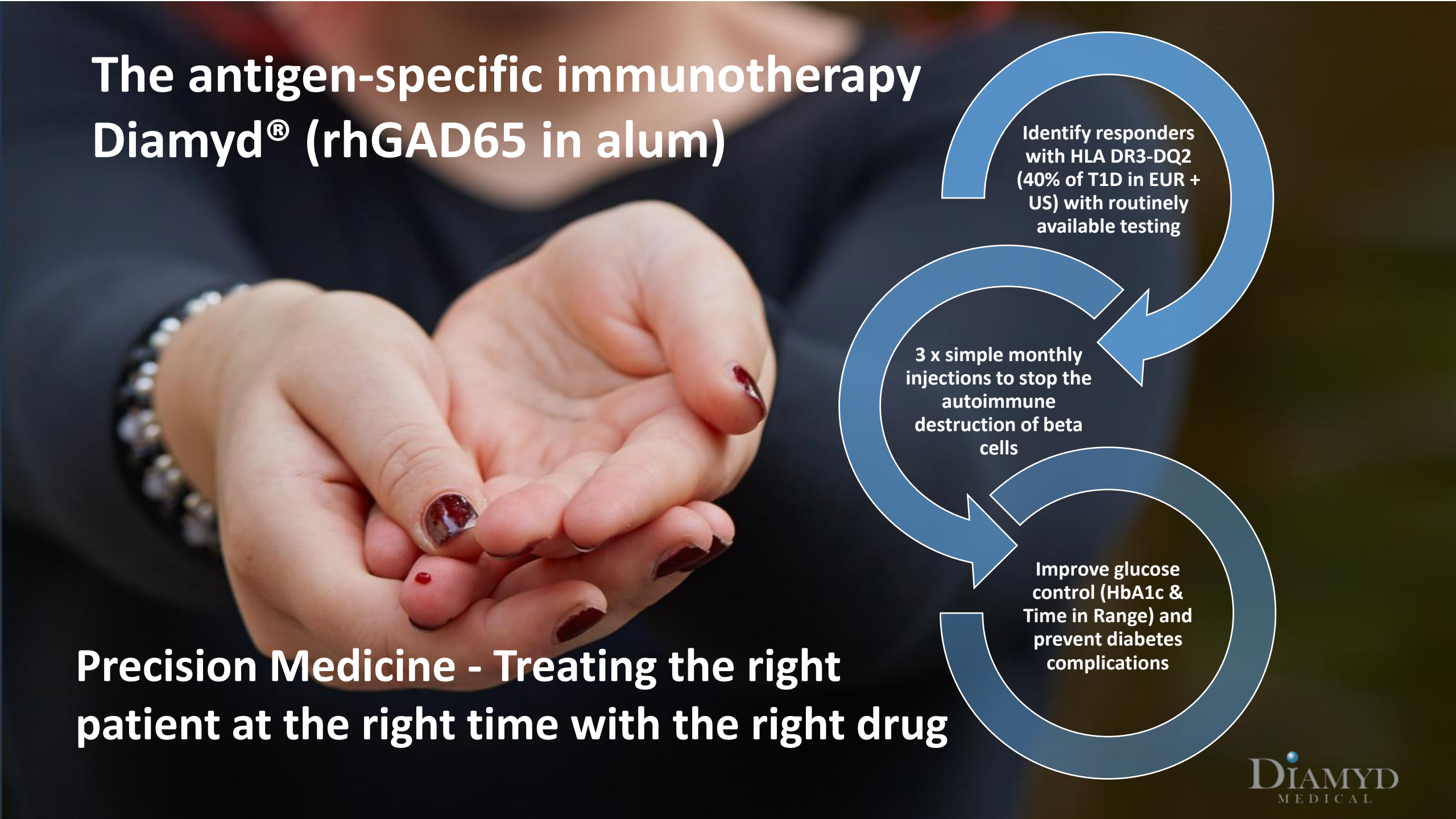
The antigen-specific immunotherapy Diamyd® (rhGAD65 in alum)



Precision Medicine - Treating the right patient at the right time with the right drug

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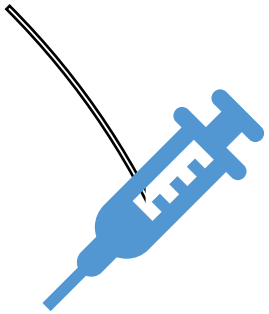
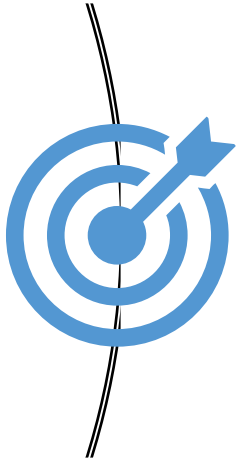
Diamyd® (rhGAD65/alum)

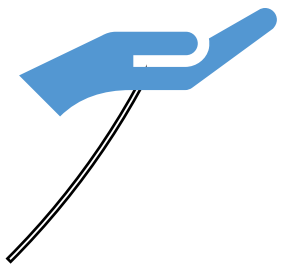
Targeting the Root Cause of Autoimmune Diabetes



Three convenient out-patient administrations only, renders **long-term effect**. Strong safety profile, **no immunosuppression**. Evaluated in around 1,000 persons with Stage 1, 2 & 3 T1D as well as in LADA



Precision medicine for individuals with specific HLA genetic marker. Approximately 40% of those living with T1D carry the marker



Accelerated Approval pathway – early read-out of registrational study expected ~March 2026. FDA Fast Track Designation for Stage 1, 2 and 3 T1D, U.S. Orphan Designation. Unique clinical and commercial potential

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Significant Momentum Paves Way for Potential Accelerated Approval

March 2022
Phase III starts

DIAGNODE-3 is initiated in Europe and expands to the US in September 2023

February 2024
Fast Track Stage 3 T1D

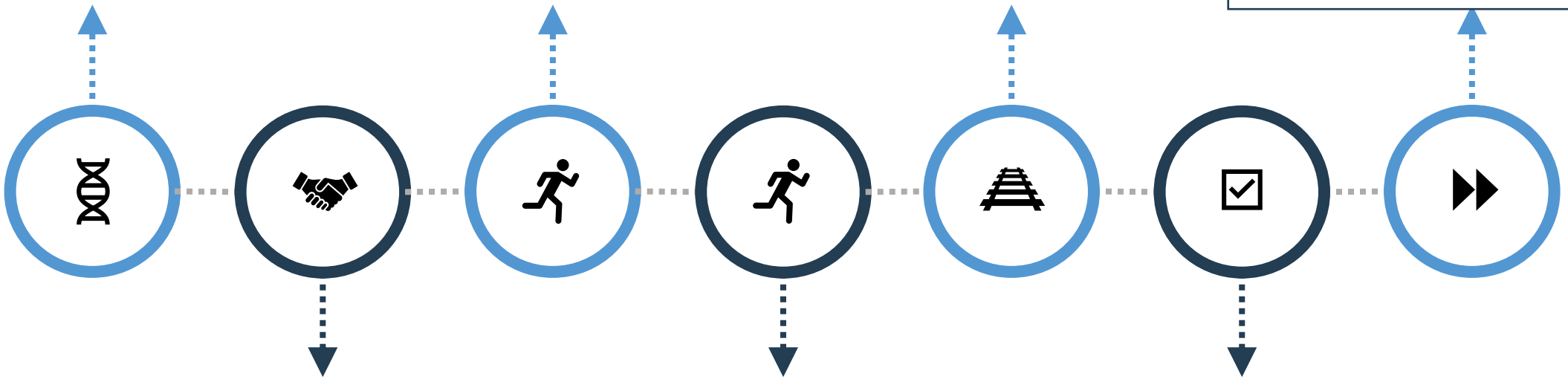
FDA grants Fast Track designation for Diamyd® to improve glycemic control in Stage 3 T1D

July 2024
Accelerated pathway

FDA acknowledges in Type C meeting C-peptide as surrogate endpoint for accelerated approval for Diamyd®

Present
Focus on expedited approval

Potential for accelerated approval including priority and rolling review. Interim readout planned for March 2026.



April 2023
Breakthrough T1D partnership

Partnership signed for financial support, awareness and regulatory support for DIAGNODE-3

June 2024
Fast Track Stage 1 & 2 T1D

FDA grants Fast Track designation for Diamyd® to treat Stage 1 & 2 T1D

July 2024
Positive interim analysis

DIAGNODE-3 successfully shows non-futility with DSMB recommendation to continue the trial unmodified

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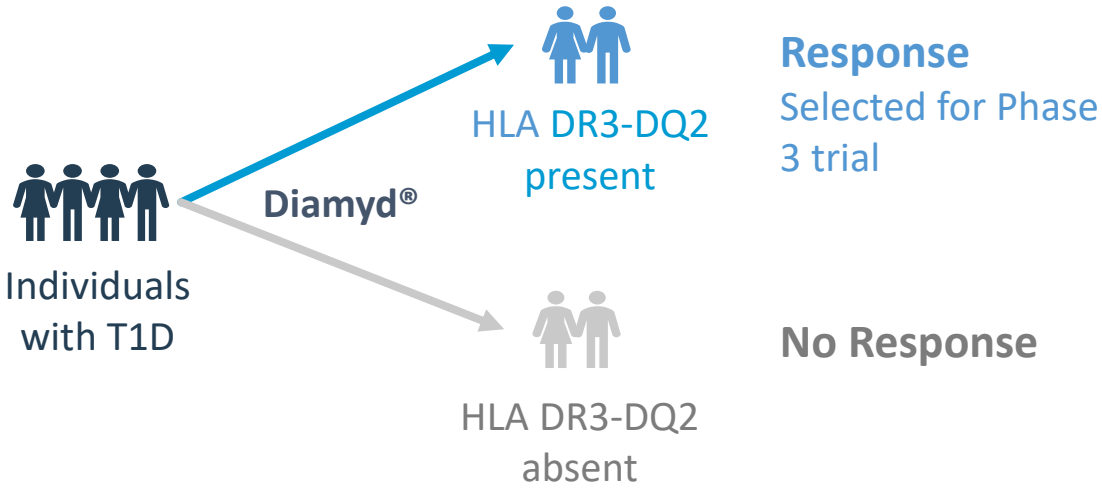
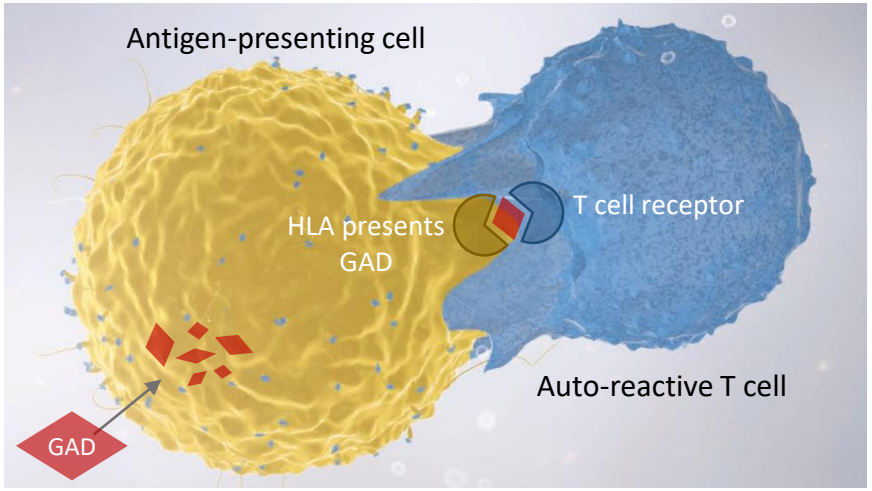
Diamyd® targets the GADA-first T1D endotype with HLA DR3-DQ2 positivity



Response
Selected for Phase 3 trial

No Response

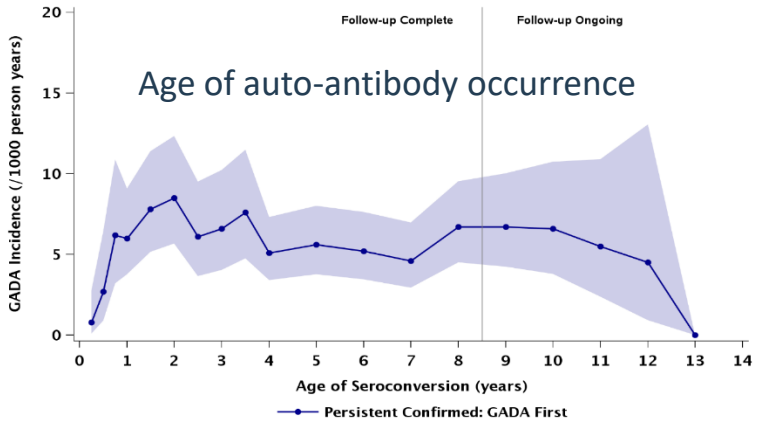


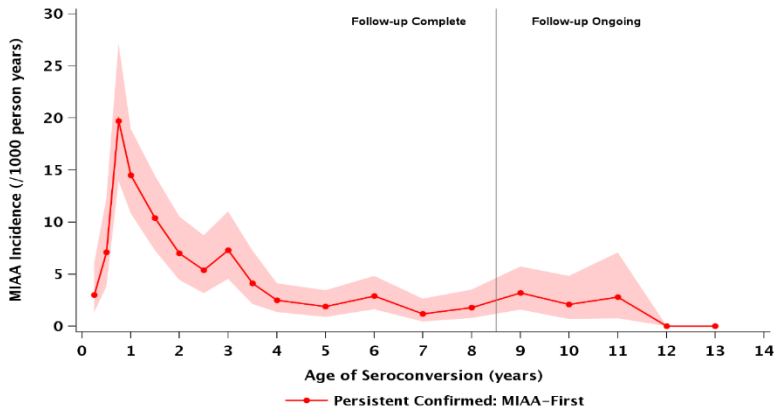
HLA is central to autoimmunity against GAD

Diamyd® responders

GADA-first disease

- HLA DR3-DQ2 (40%)
- Adenovirus F
- *BACH2*
- Likely responders to Diamyd®





IAA-first disease

- HLA DR4-DQ8 (60%)
- Enterovirus B
- *INS , PTPN22, UBASH3A*
- Likely responders to an insulin-based antigen-specific therapy

Courtesy of Prof. Åke Lernmark. Graphs based on data from the TEDDY study.

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Acknowledged Precision Medicine approach

Highlights

- New medical consensus regarding genetically defined groups of T1D
- Strong case for a precision medicine approach targeting likely responders
- Diamyd Medical's approach is to focus on individuals with GAD antibodies and HLA DR3-DQ2 (40% of US + EU T1D) based on
  - Identification of this responder population in previous clinical trials with Diamyd®
  - A biological rationale as HLA DR3-DQ2 is associated with primary autoimmunity against GAD65 (the active component of Diamyd®)

Diabetes Care Volume 43, January 2020 5

Check for updates

Introducing the Endotype Concept to Address the Challenge of Disease Heterogeneity in Type 1 Diabetes

Diabetes Care 2020;43:5–12 | https://doi.org/10.2337/dc19-0880

Manuela Battaglia,[1] Simi Ahmed,[2] Mark S. Anderson,[3] Mark A. Atkinson,[4] Dorothy Becker,[5] Polly J. Bingley,[6] Emanuele Bosi,[1,7] Todd M. Brusko,[4] Linda A. DiMeglio,[8] Carmella Evans-Molina,[9] Stephen E. Gitelman,[10] Carla J. Greenbaum,[11] Peter A. Gottlieb,[12] Kevan C. Herold,[13] Martin J. Hessner,[14] Mikael Knip,[15] Laura Jacobsen,[16] Jeffrey P. Krischer,[17] S. Alice Long,[11] Markus Lundgren,[18] Eoin F. McKinney,[19] Noel G. Morgan,[20,21] Richard A. Oram,[22,23,24] Tomi Pastinen,[25] Michael C. Peters,[26] Alessandra Petrelli,[1] Xiaoning Qian,[27] Maria J. Redondo,[28] Bart O. Roep,[29,30] Desmond Schatz,[16] David Skibinski,[11] and Mark Peakman[31,32]

Battaglia et al, Introducing the endotype concept to address the challenge of disease heterogeneity in type 1 diabetes, Diabetes Care, 2020

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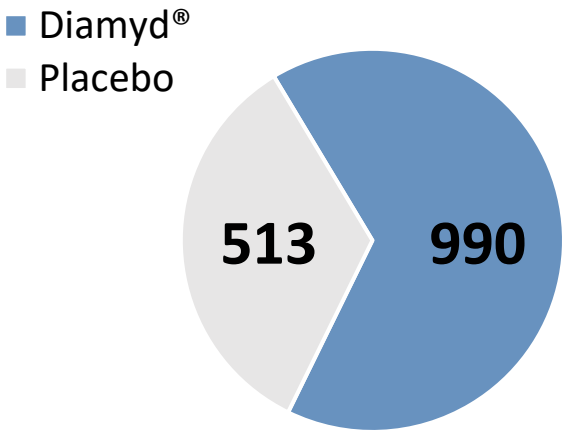
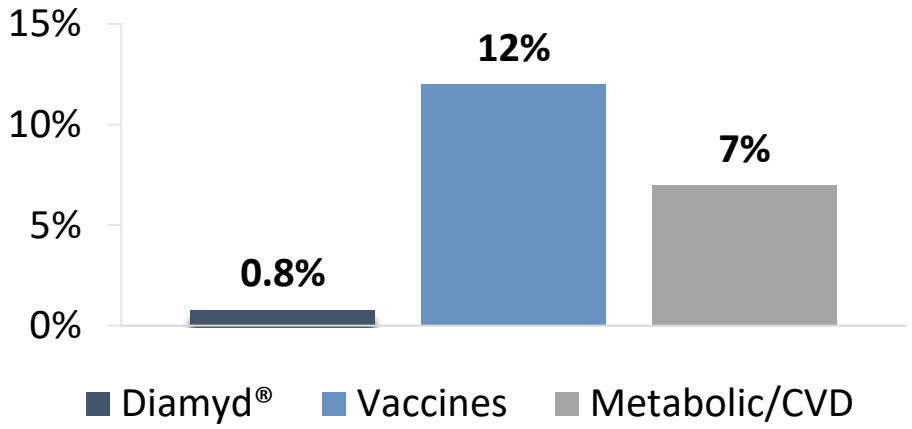
Very Good Safety and Tolerability Profile

No major safety signals in >990 patients exposed to Diamyd®. Drop-out rate <1% across 15 clinical trials.

Total patient exposure in 15 trials



Patient drop-out rate in clinical trials



Summary of clinical safety data

- Most common adverse events: transient tenderness at injection site, injection site edema, mild injection site pain and injection site reaction
- No difference in the rate of occurrence of adverse events between active Diamyd® and placebo treatment
- No major safety signals in 15 clinical trials
- <1% drop-out rate across trials
- Assessed in persons aged 4 – 70 years
- Assessed in persons with T1D, LADA and healthy persons at-risk of developing T1D

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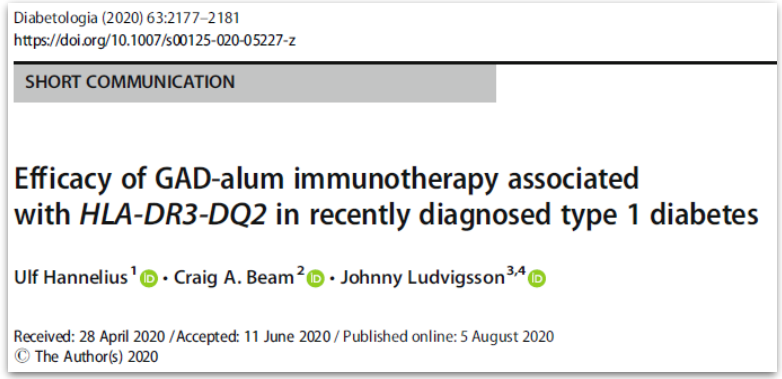
Meta-analysis of 3 pre-2014 Trials Identified Responder Patients

Meta-analysis of 3 randomized controlled clinical trials with subcutaneous Diamyd® conducted before 2014 with >500 individuals identified patients carrying HLA DR3-DQ2 gene as responders

44% reduction in C-peptide decline

from Baseline to Month 15 compared to placebo in patients carrying the HLA DR3-DQ2 gene who received 3 or 4 iniections of Diamyd®



Diabetologia (2020) 63:2177–2181
https://doi.org/10.1007/s00125-020-05227-z

SHORT COMMUNICATION

Efficacy of GAD-alum immunotherapy associated with *HLA-DR3-DQ2* in recently diagnosed type 1 diabetes

Ulf Hannelius[1] · Craig A. Beam[2] · Johnny Ludvigsson[3,4]

Received: 28 April 2020 / Accepted: 11 June 2020 / Published online: 5 August 2020
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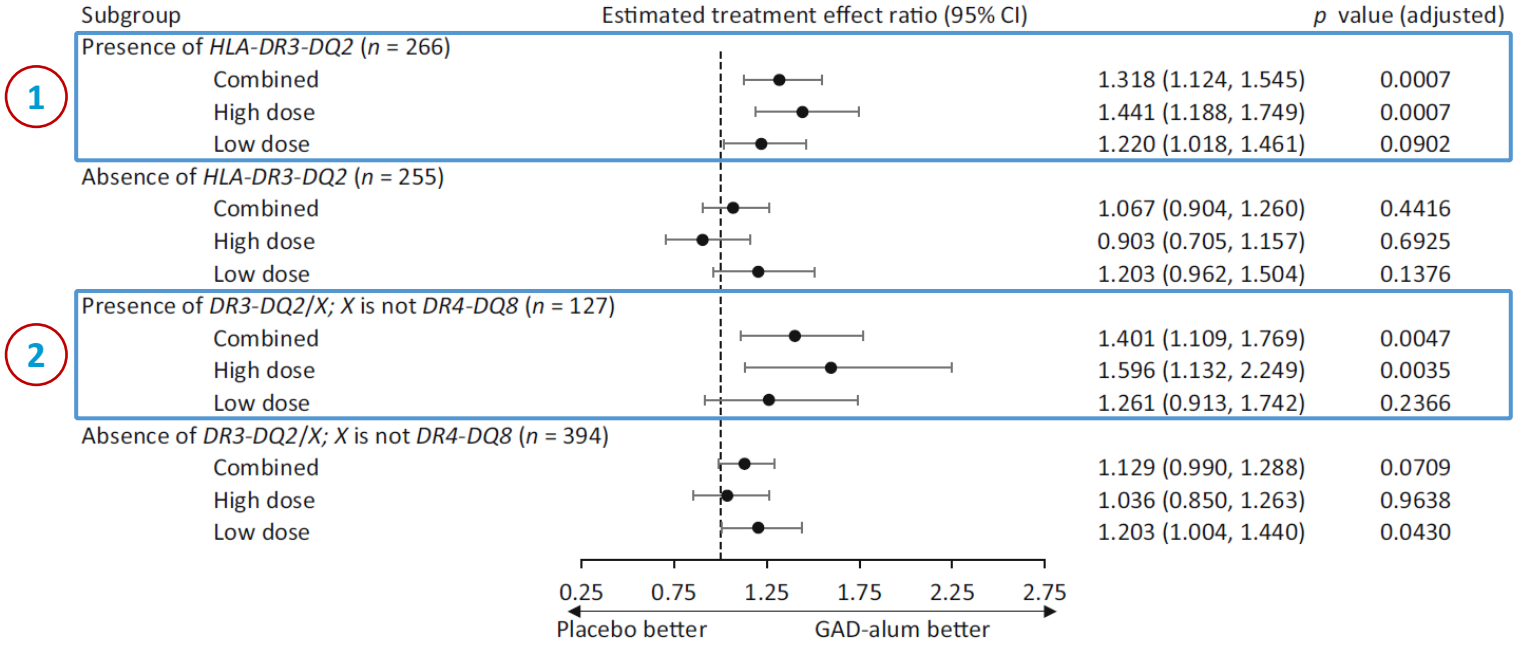
Hannelius et al. Diabetologia 2020

Mixed meal tolerance test (MMTT) stimulated C-peptide



High dose = 3 or 4 injections; Low dose = 2 injections; Combined = 2, 3 or 4 injections

1 **Significant treatment effect in subgroup of patients positive for HLA DR3-DQ2 gene (responder patients)**

2 **Even larger treatment effect in ca. 50% of responder patients with HLA DR3-DQ2 who lack the HLA DR4-DQ8 gene (super responder patients)**

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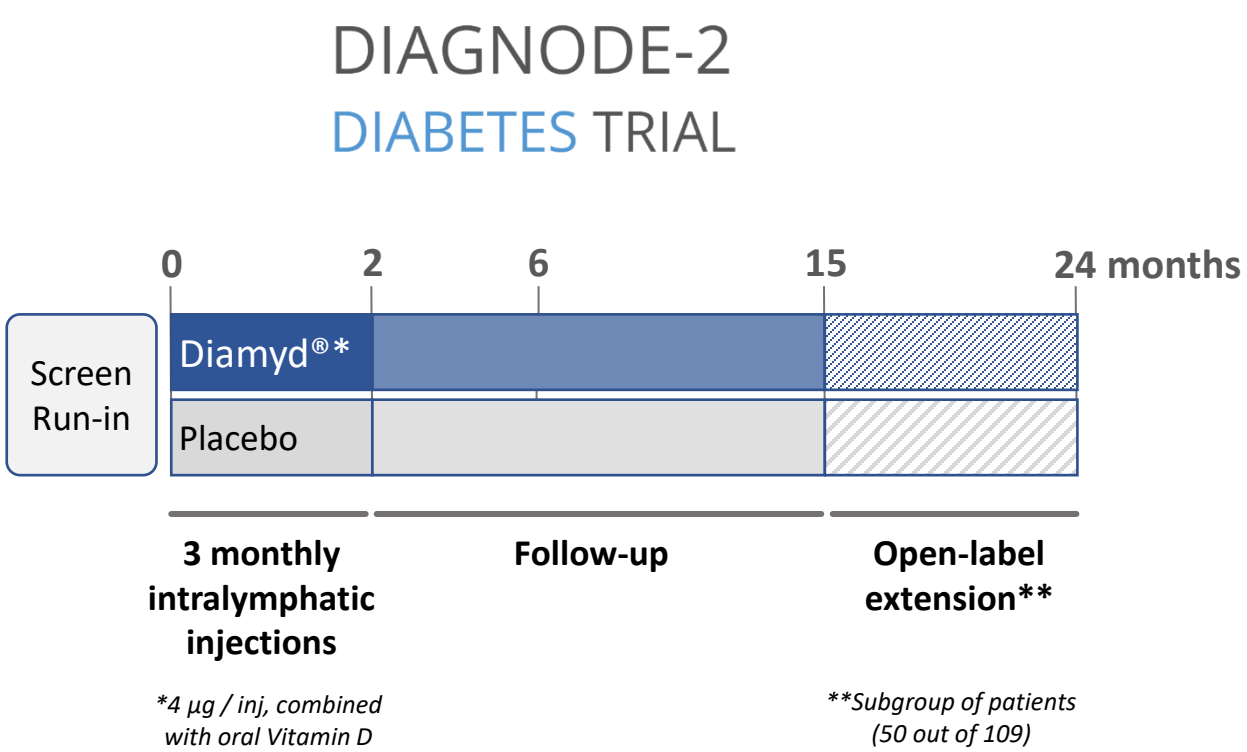
DIAGNODE-2 Phase 2b Trial Confirmed Responder Patients

European, multinational, randomized, placebo-controlled, 2-arm trial assessing 3 intralymphatic injections of Diamyd® given on top of standard of care



Primary Endpoint

- Change from Baseline to Month 15 in Mixed Meal Tolerance Test (MMTT) stimulated C-peptide Area under the Curve

Key Secondary Endpoint

- Change in Hemoglobin A1c (HbA1c) between baseline and Month 15
- Change in insulin-dose-adjusted HbA1c (IDAA1c) between Baseline and Month 15
- Change in daily exogenous insulin consumption between Baseline and Month 15

Population

- Persons diagnosed with T1D less than 6 months ago aged 12-24 years and positive for GAD antibodies
- Residual beta cell function: fasting C-peptide ≥ 0.12 nmol/L
- Pre-specified subgroup added to topline readout before database lock: responder patients with HLA DR3-DQ2 genotype

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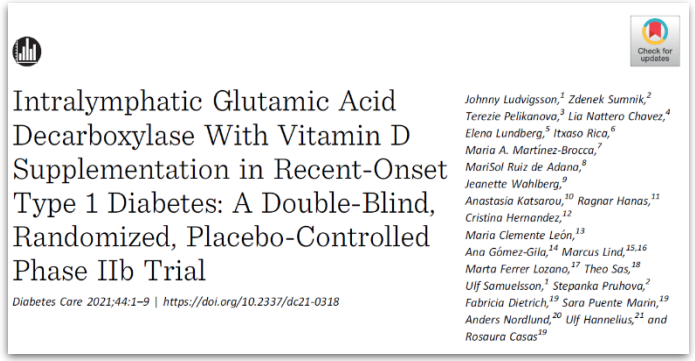
DIAGNODE-2 Phase 2b Trial Confirmed Responder Patients

Diamyd® achieved statistically significant preservation of C-peptide secretion, numerical improvement in HbA1c compared to placebo at Month 15 in patients with HLA DR3-DQ2

56% reduction in C-peptide decline

from Baseline to Month 15 compared to placebo treatment in patients carrying the HLA DR3-DQ2 gene



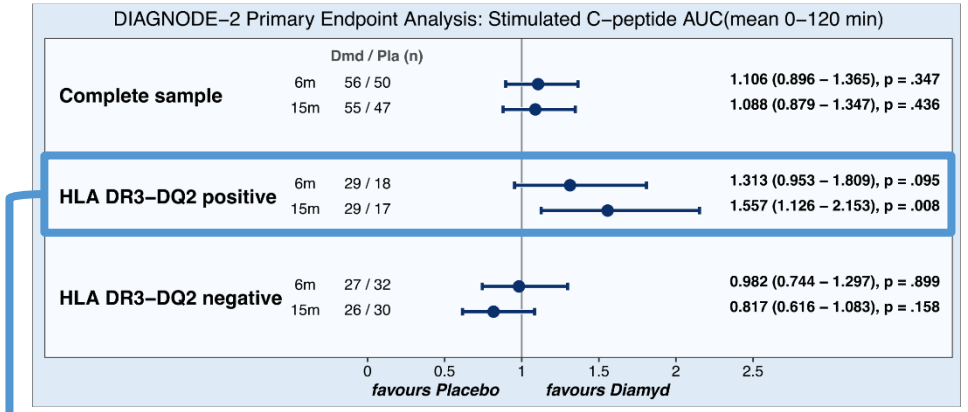
Intralymphatic Glutamic Acid Decarboxylase With Vitamin D Supplementation in Recent-Onset Type 1 Diabetes: A Double-Blind, Randomized, Placebo-Controlled Phase IIb Trial

Diabetes Care 2021;44:1–9 | https://doi.org/10.2337/dc21-0318

Johnny Ludvigsson,[1] Zdenek Sumnik,[2] Terezie Pelikanova,[3] Lia Nattero Chavez,[4] Elena Lundberg,[5] Itxaso Rica,[6] Maria A. Martinez-Brocca,[7] MariSol Ruiz de Adana,[8] Jeanette Wahlberg,[9] Anastasia Katsarou,[10] Ragnar Hanas,[11] Cristina Hernandez,[12] Maria Clemente León,[13] Ana Gómez-Gila,[14] Marcus Lind,[15,16] Marta Ferrer Lozano,[17] Theo Sas,[18] Ulf Samuelsson,[1] Stepanka Pruhova,[2] Fabricia Dietrich,[19] Sara Puente Marin,[19] Anders Nordlund,[20] Ulf Hannelius,[21] and Rosaura Casas[19]

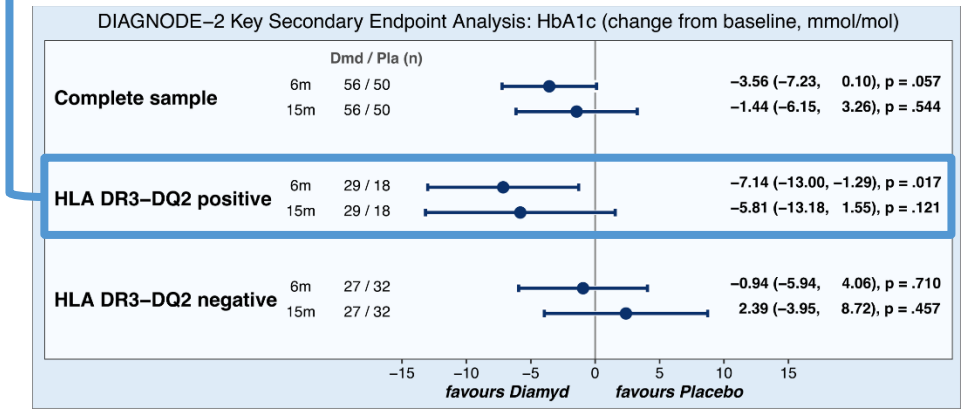
Ludvigsson et al. Diabetes Care 2021

Mixed meal tolerance test (MMTT) stimulated C-peptide



Pre-specified subgroup of patients positive for HLA DR3-DQ2 gene

Glycated haemoglobin (HbA1c)



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DIAGNODE-2 Phase 2b trial Confirmed Responder Patients

In exploratory analyses, Diamyd® achieved statistically significant benefit on Continuous Glucose Monitoring (CGM) outcomes in patients carrying the HLA DR3-DQ2 responder gene

Better Time in Range, glycaemic variability, time in severe hyperglycaemia


JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

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Article Contents

Abstract

ACCEPTED MANUSCRIPT

Intralymphatic GAD-alum (Diamyd®) improves glycaemic control in Type 1 diabetes with HLA DR3-DQ2

Christoph Nowak, MD, PhD, Marcus Lind, MD PhD, Zdenek Sumnik, MD, Terezie Pelikanova, MD, Lia Nattero Chavez, MD, PhD, Elena Lundberg, MD, PhD, Itxaso Rica, MD, Maria A Martinez-Brocca, MD, PhD, Mari Sol Ruiz de Adana, MD, Jeanette Wahlberg, MD, PhD ... Show more

Nowak et al. JCEM 2022


JOURNAL ARTICLE

Antigen-based Immunotherapy Improves Glycemic Metrics and β-Cell Function Get access >

Maria Elena Lunati, Paolo Fiorina

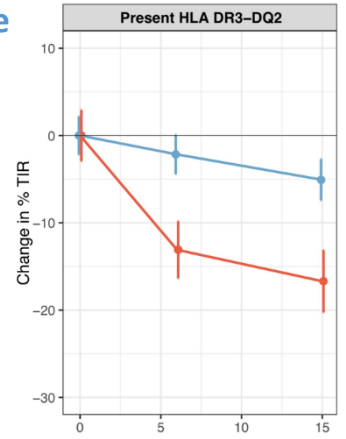
The Journal of Clinical Endocrinology & Metabolism, Volume 107, Issue 10, October 2022, Pages e4250–e4251, https://doi.org/10.1210/clinem/dgac437

Published: 26 July 2022 **Article history**

Independent Commentary by Lunati & Fiorina, JCEM 2022

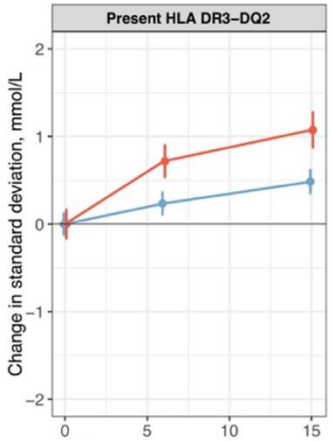
Time in Range

% change from Baseline to Month 15



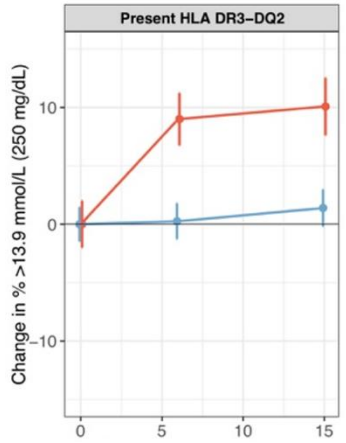
Glycaemic variability

Change in standard deviation from Baseline to Month 15



Time in severe hyperglycaemia

>250 mg/dL (>13.9 mmol/L) % change from Baseline to Month 15



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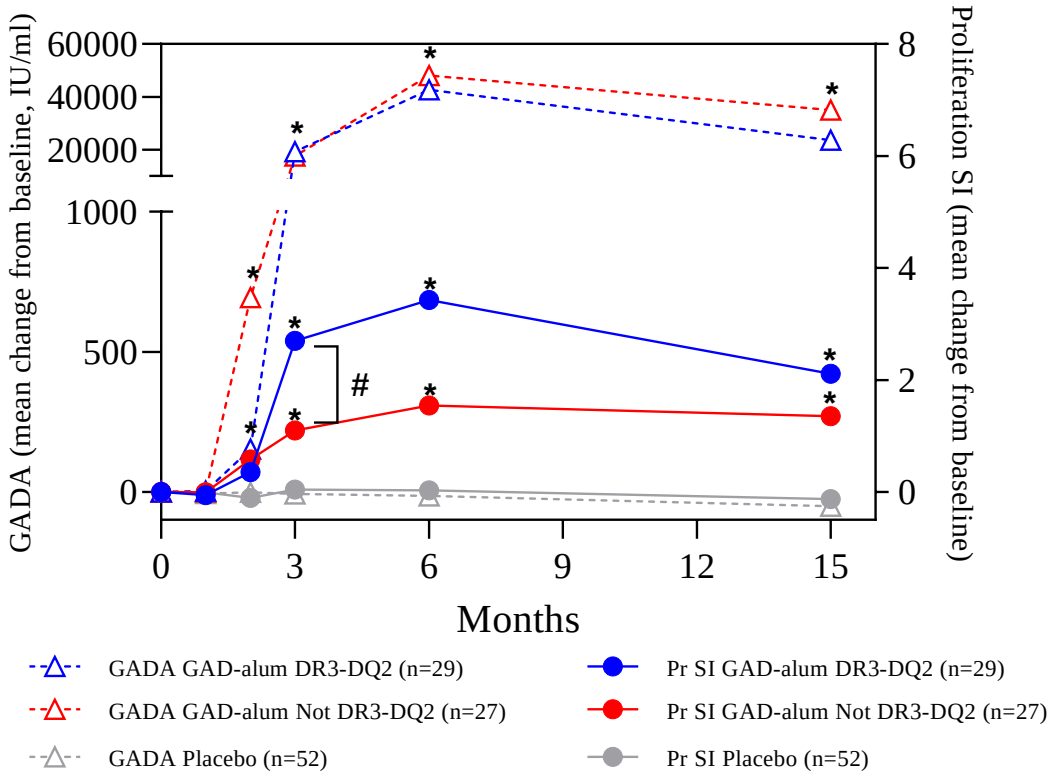
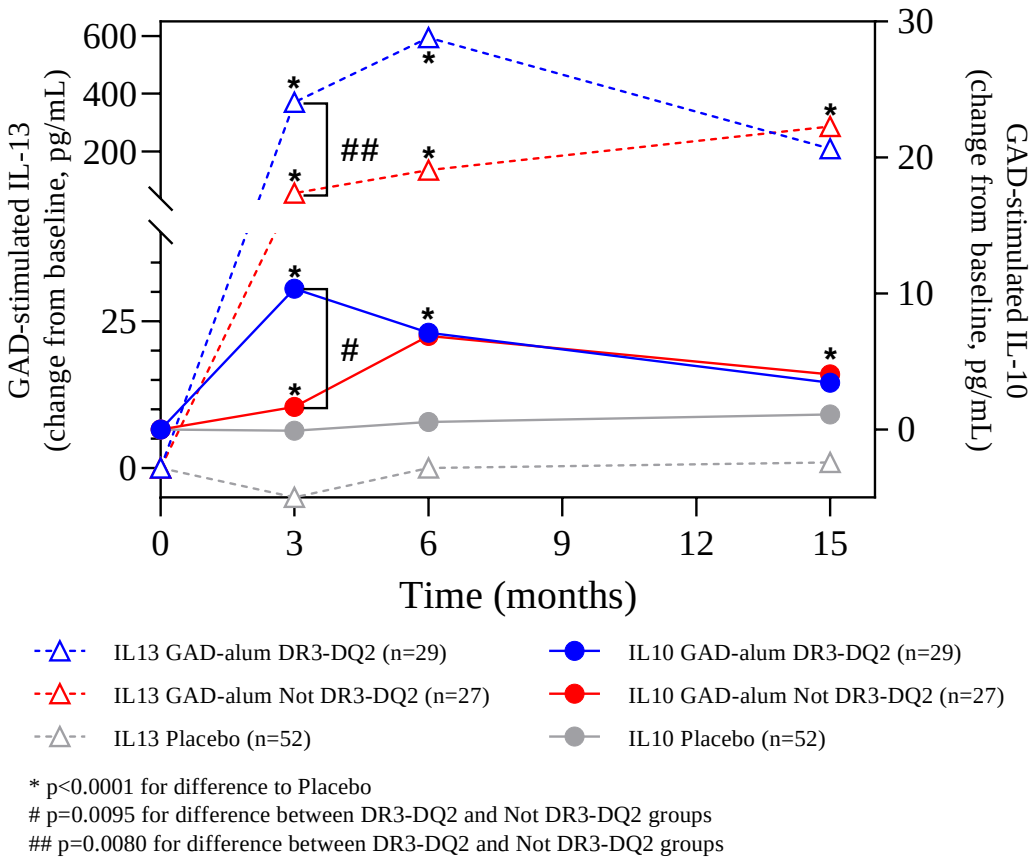
DIAGNODE-2 Phase 2b trial biomarker data support HLA-specific response

GADA, proliferation and cytokine secretion



* p<0.001 for difference to Placebo
# p=0.0210 for difference between DR3-DQ2 and Not DR3-DQ2 groups



* p<0.0001 for difference to Placebo
# p=0.0095 for difference between DR3-DQ2 and Not DR3-DQ2 groups
p=0.0080 for difference between DR3-DQ2 and Not DR3-DQ2 groups

Median change from baseline of anti-GAD65 antibodies (GADA) and Proliferation of PMBC (Stimulation Index, SI) *(A)*, and GAD-stimulated secretion by PBMC of IL-10 and IL-13 levels *(B)* for GAD-alum treated subjects with and without the DR3-DQ2 haplotype Placebo treatment subjects.

P values, Wilcoxon test, are indicated.

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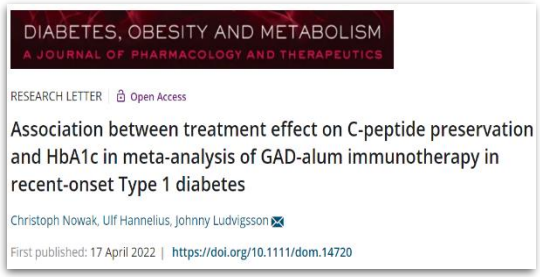
Correlated Diamyd® Treatment Effects on C-peptide and HbA1c

Updated meta-analysis including the Phase 2b trial strengthens conclusion about patients carrying the HLA DR3-DQ2 gene being Diamyd® treatment responders and shows correlated treatment effects on C-peptide and HbA1c – the two co-primary endpoints of the Phase 3 trial

48% reduction in C-peptide decline, 4.8 mmol/mol (0.5% DCCT units) lower HbA1c

from Baseline to Month 15 compared to placebo in patients carrying the HLA DR3-DQ2 gene who received 3 or 4 iniections of Diamyd®


DIABETES, OBESITY AND METABOLISM
A JOURNAL OF PHARMACOLOGY AND THERAPEUTICS

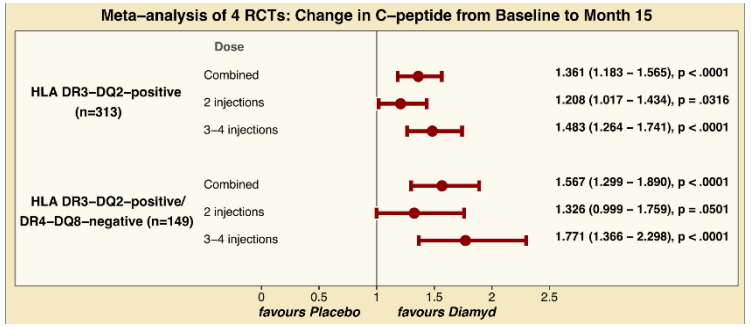
RESEARCH LETTER | Open Access

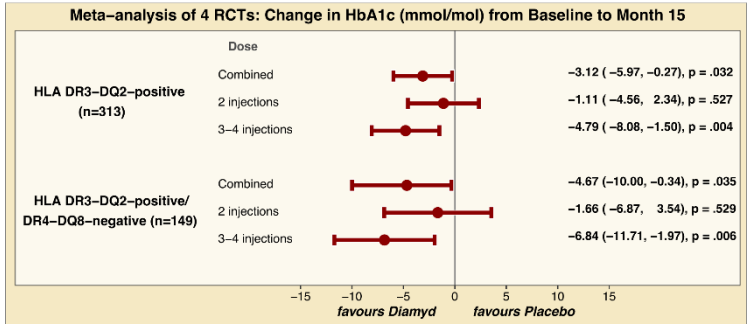
Association between treatment effect on C-peptide preservation and HbA1c in meta-analysis of GAD-alum immunotherapy in recent-onset Type 1 diabetes

Christoph Nowak, Ulf Hannelius, Johnny Ludvigsson

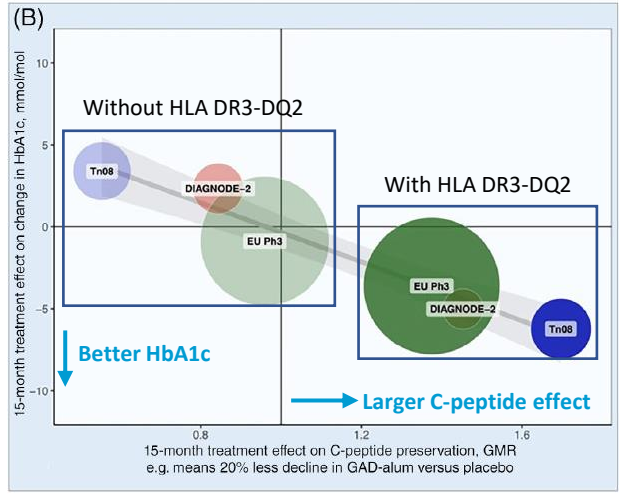
First published: 17 April 2022 | https://doi.org/10.1111/dom.14720

Nowak et al. Diabetes Obesity and Metabolism 2022





3 or 4 doses of Diamyd® vs placebo

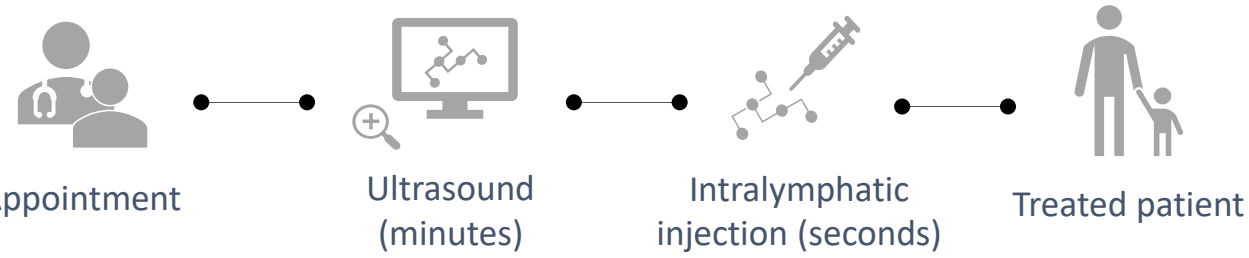


The figure shows individual trial samples of patients with recent-onset T1D divided into present/absent HLA DR3-DQ2 who received 3 or 4 injections of Diamyd® or placebo. It is shows a correlation between larger treatment benefit on C-peptide (x-axis; further to the right means larger benefit of Diamyd® over placebo) and lower HbA1c (y-axis, further negative means lower HbA1c and larger benefit of Diamyd® over placebo). All effects refer to change from Baseline to Month 15.

DIAMYD MEDICAL

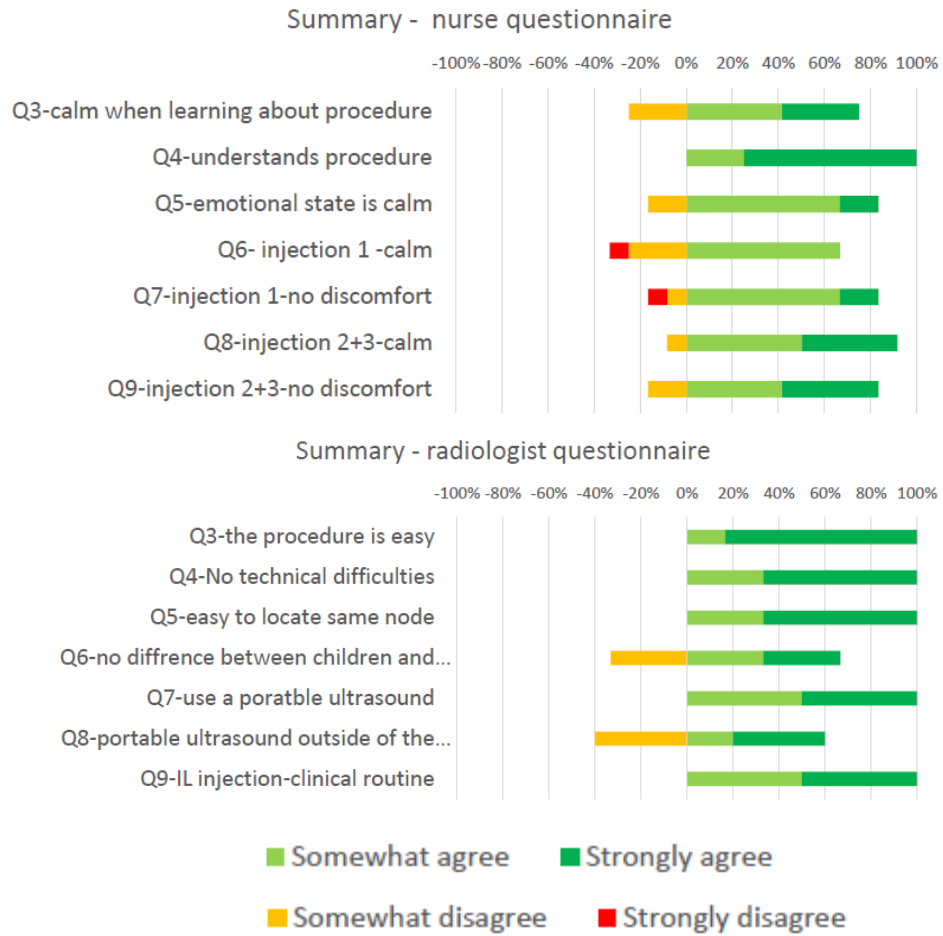
Ultrasound-guided intralymphatic injection

Quick, low-key outpatient procedure with discomfort comparable to venepuncture



- Procedure performed by a **radiologist** or **trained professional**
- **Strong interest from endocrinologists to learn the procedure:** traditionally “underpaid” specialisty in US; eager to add utrasound training to procedural skillset; potential for certification and collaboration with US endocrinology societies
- **Three ultrasound guided injections** in a groin lymph node, one month apart
- **Safe** procedure, assessed in 12-28-year-old (DiaPrecise prevention trial will enrol Stage 1/2 children down to 8 years of age)
- Pain level equal to taking a blood sample

HCP feedback in DIAGNODE-2

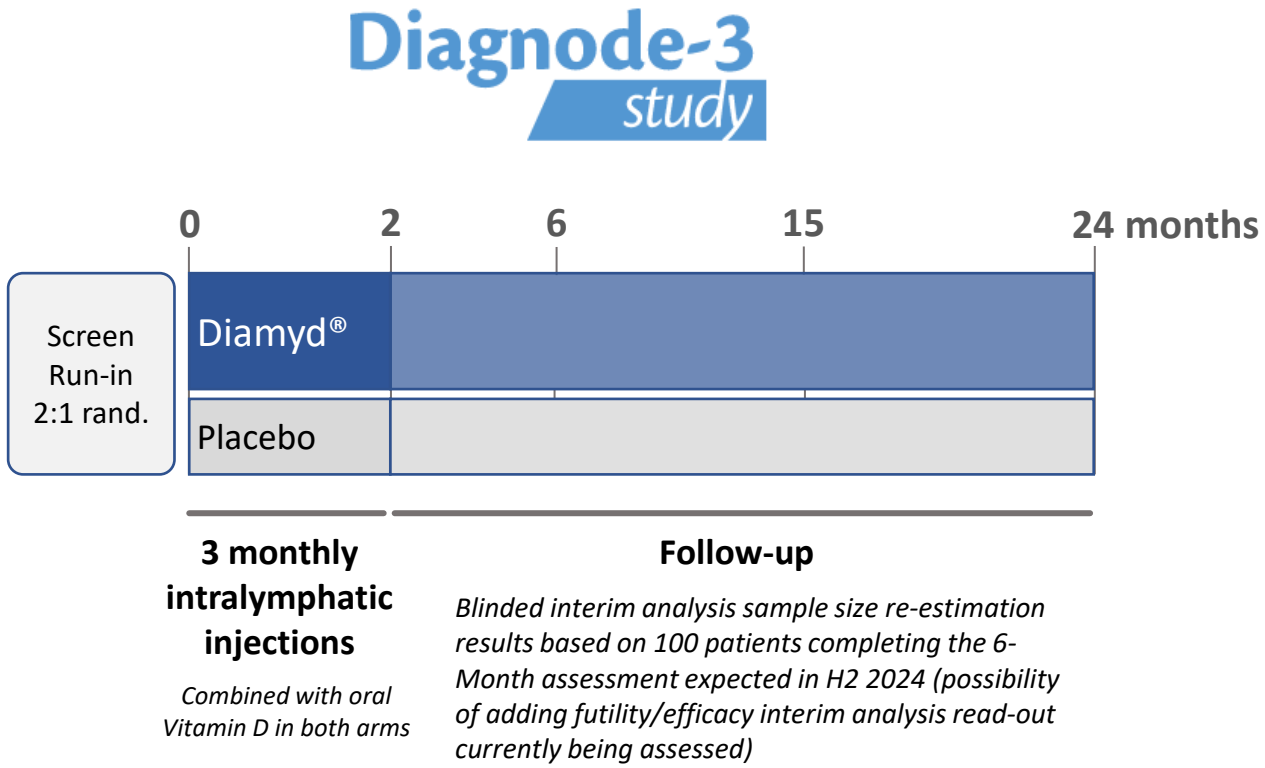


Selam Dessehaye. Evaluation of the feasibility of intralymphatic injection of Diamyd. Master Thesis. Uppsala University, Uppsala, Sweden. June 25, 2019.

DIAMYD MEDICAL

DIAGNODE-3 Pivotal Precision Medicine Phase 3 trial

Multinational (EU + US), randomized, placebo-controlled, 2-arm trial assessing 3 intralymphatic injections of Diamyd® given on top of standard of care. Designed based on Phase 2b trial in alignment with FDA and EMA. Enrolling only likely responder patients carrying the HLA DR3-DQ2 gene.



Co-Primary Endpoints

- Stimulated C-peptide area under the curve, change from Baseline to Month 24 in Mixed Meal Tolerance Test (MMTT)
- HbA1c, change from Baseline to Month 24

Secondary Endpoints

- Time in glycemic target range 3.9-10 mmol/L (70-180 mg/dL) assessed by CGM, change from Baseline to Month 24
- Proportion of patients with insulin dose-adjusted HbA1c (IDAA1c) ≤9 (partial remission) at Month 24
- Number of episodes per patient of severe hypoglycemia between Baseline and Month 24
- Number of episodes per patient of diabetic ketoacidosis (DKA) between Baseline and Month 24

Population

- Persons diagnosed with T1D less than 6 months ago aged 12-29 years who are positive for GAD antibodies and positive for HLA DR3-DQ2
- Residual beta cell function: fasting C-peptide ≥ 0.12 nmol/L

DIAMYD MEDICAL

DIAGNODE-3 Pivotal Precision Medicine Phase 3 trial

Ongoing at just over 50 clinical sites in Europe

Ongoing at around a dozed clinical sites in the US

In partnership with

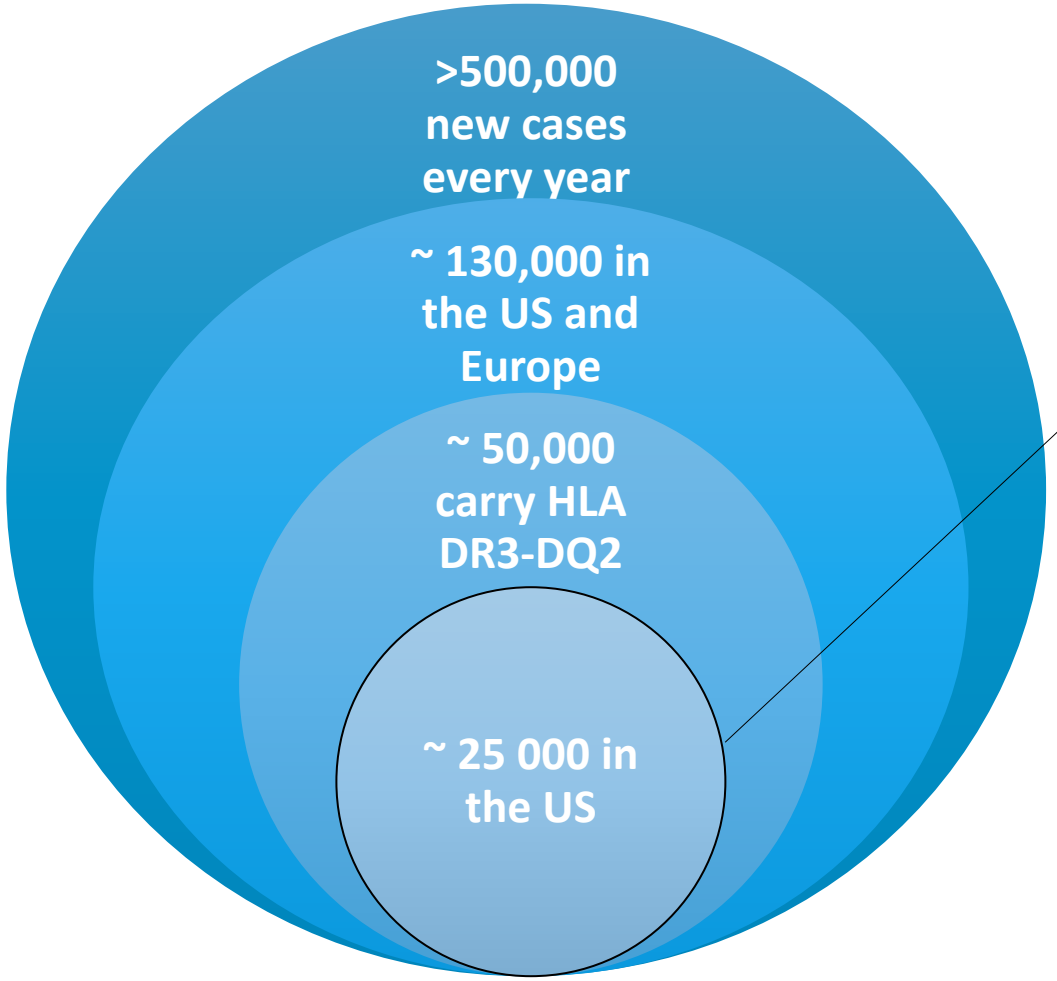
Breakthrough T1D™
Formerly JDRF

www.diagnode-3.com

DIAMYD MEDICAL

$5 Billion Addressable Market in the US Alone

Lead indication: Treatment of Stage 3 Type 1 Diabetes



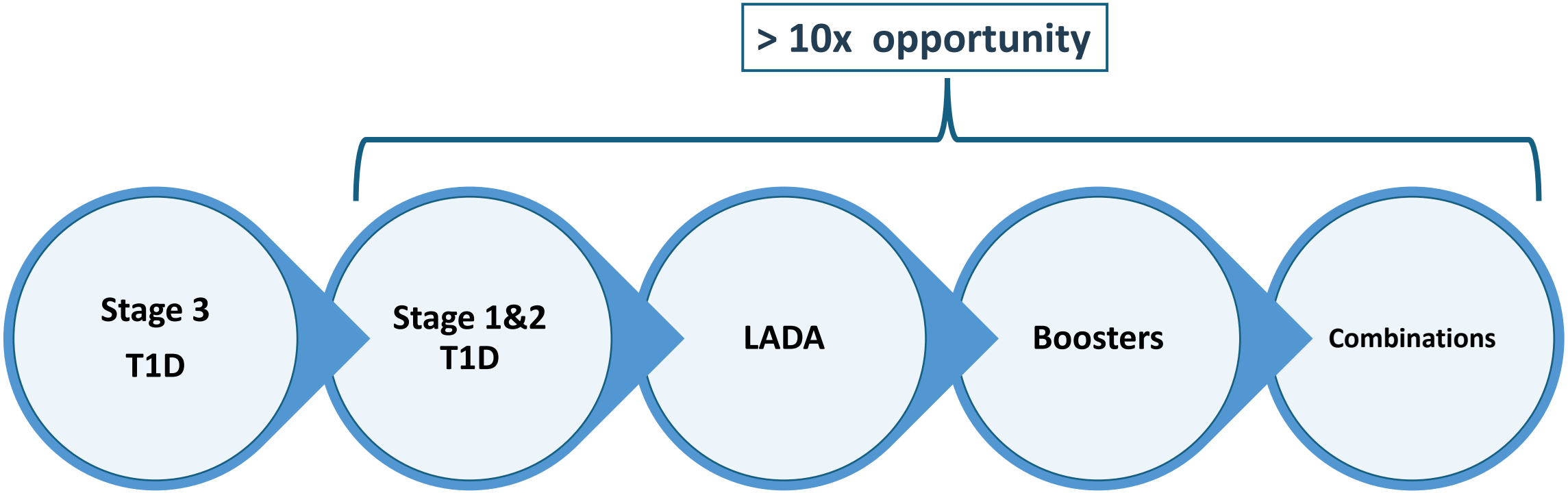
- The **US T1D market** represents over **$5 billion** in addressable opportunity, driven by a high incidence, unmet needs in disease management and ~ **$200,000** per treatment supported by US payers
- This unique **first-in-class** approach could capture a large market share due to its superior safety profile, long-term efficacy and precision medicine approach.
- **Market exclusivity** through **US orphan designation** and **biologics exclusivity** enhance the commercial potential of Diamyd® in the US and globally.
- **Accelerated approval pathway** pursued following significant regulatory advances

Note: Assuming treatment of prevalent cases with residual beta cell function doubles the number of patients and consequently the market opportunity.

DIAMYD MEDICAL

Significant Label Expansion Opportunities

Supported by **Fast Track designation** for Stage 1, 2 & 3 T1D as well as **safety** and **proof-of-concept** clinical **efficacy** from **LADA** patients up to the age of 70 and booster injections, Diamyd® is, currently as the only therapeutic in the world, indicated across the autoimmune diabetes spectrum. This provides **significant opportunities** beyond the initial USD 5 billion Stage 3 T1D market in the United States.



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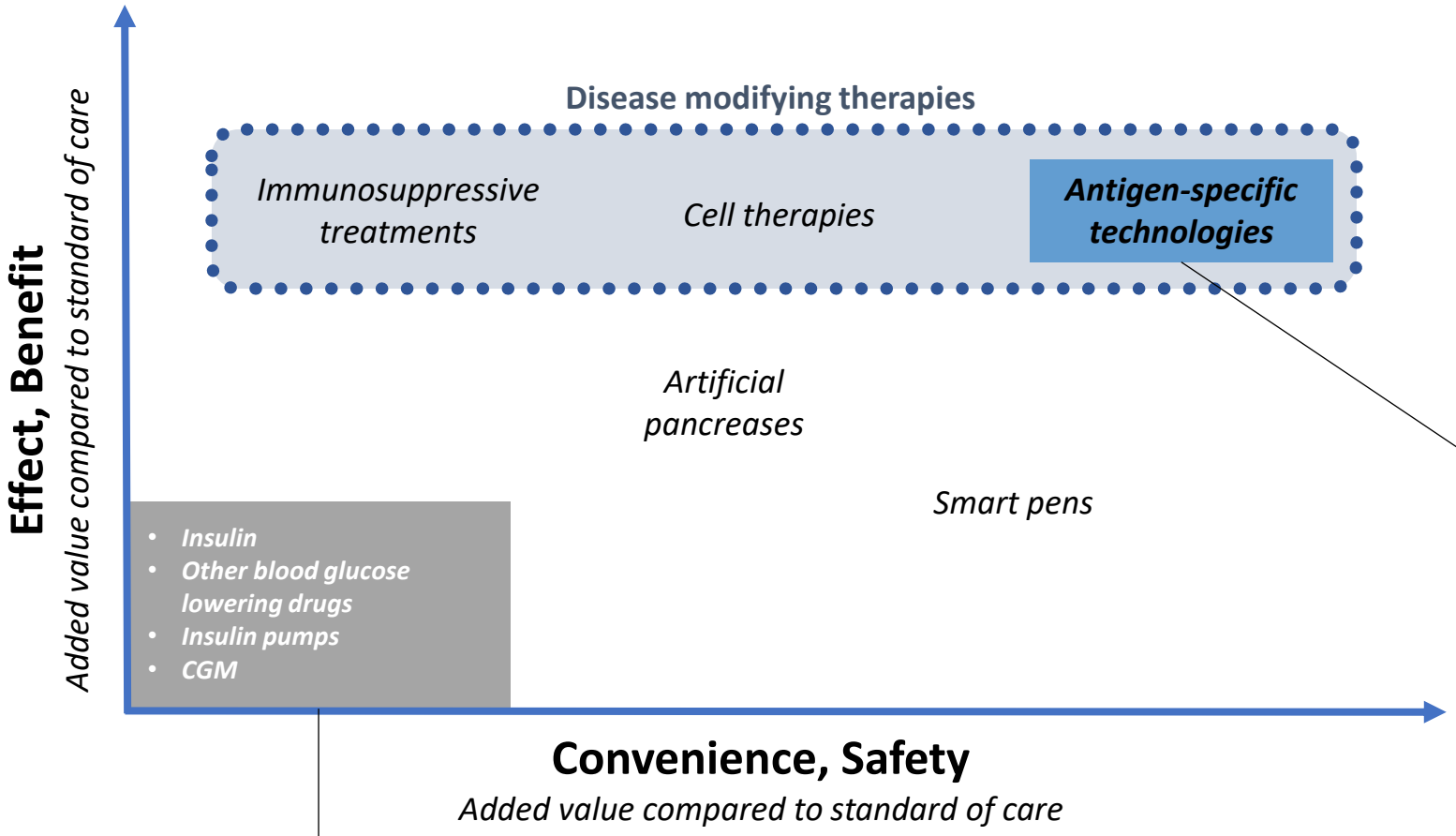
POSITION DIAMYD® TO MAXIMIZE EFFICACY, SAFETY, CONVENIENCE



Antigen-specific immunotherapy with Diamyd® targets the body's immune system by reprogramming it to stop attacking the insulin-producing cells. This treatment has the potential for long-term efficacy. Compared with other technologies under development often requiring hospitalization, the diabetes vaccine Diamyd® displays an excellent safety profile and is a fast and easy treatment.

The current **standard treatment** for type 1 diabetes is life-sustaining, subcutaneous deliveries of insulin by injection or pump therapy, combined with continuous glucose monitoring (CGM). In addition to non-insulin anti-diabetic drugs and aids, such as artificial pancreases and smart insulin pens to help patients manage their condition, therapies targeting the underlying causes of the disease are also being developed.

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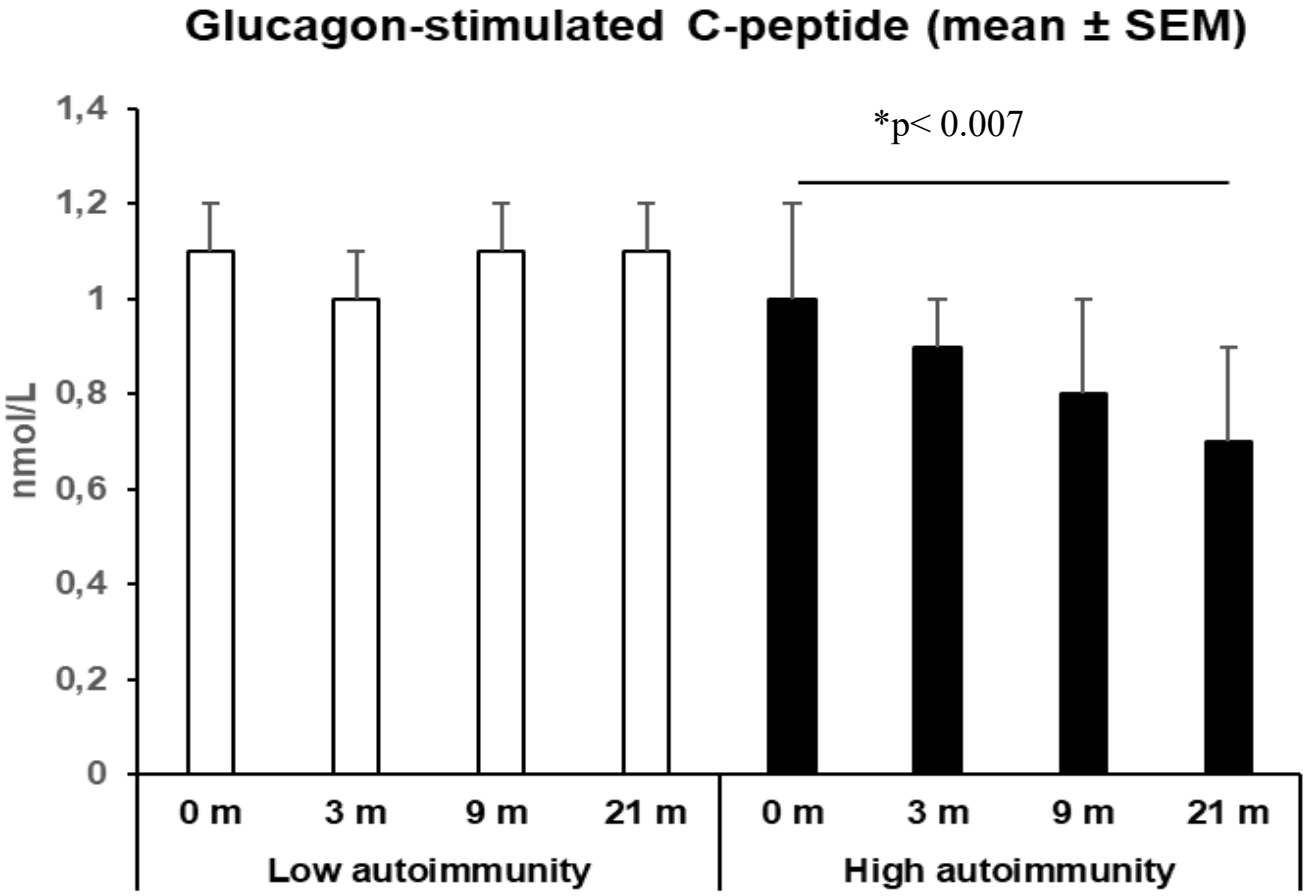
Latent Autoimmune Diabetes in Adults (LADA)*

*Also called Slowly progressing Autoimmune Diabetes (SAID) or Slowly progressing insulin-dependent diabetes mellitus (SPIDDM)

DIAMYD MEDICAL

Background

In highly autoimmune LADA individuals: treatment that directly targets autoimmunity is needed

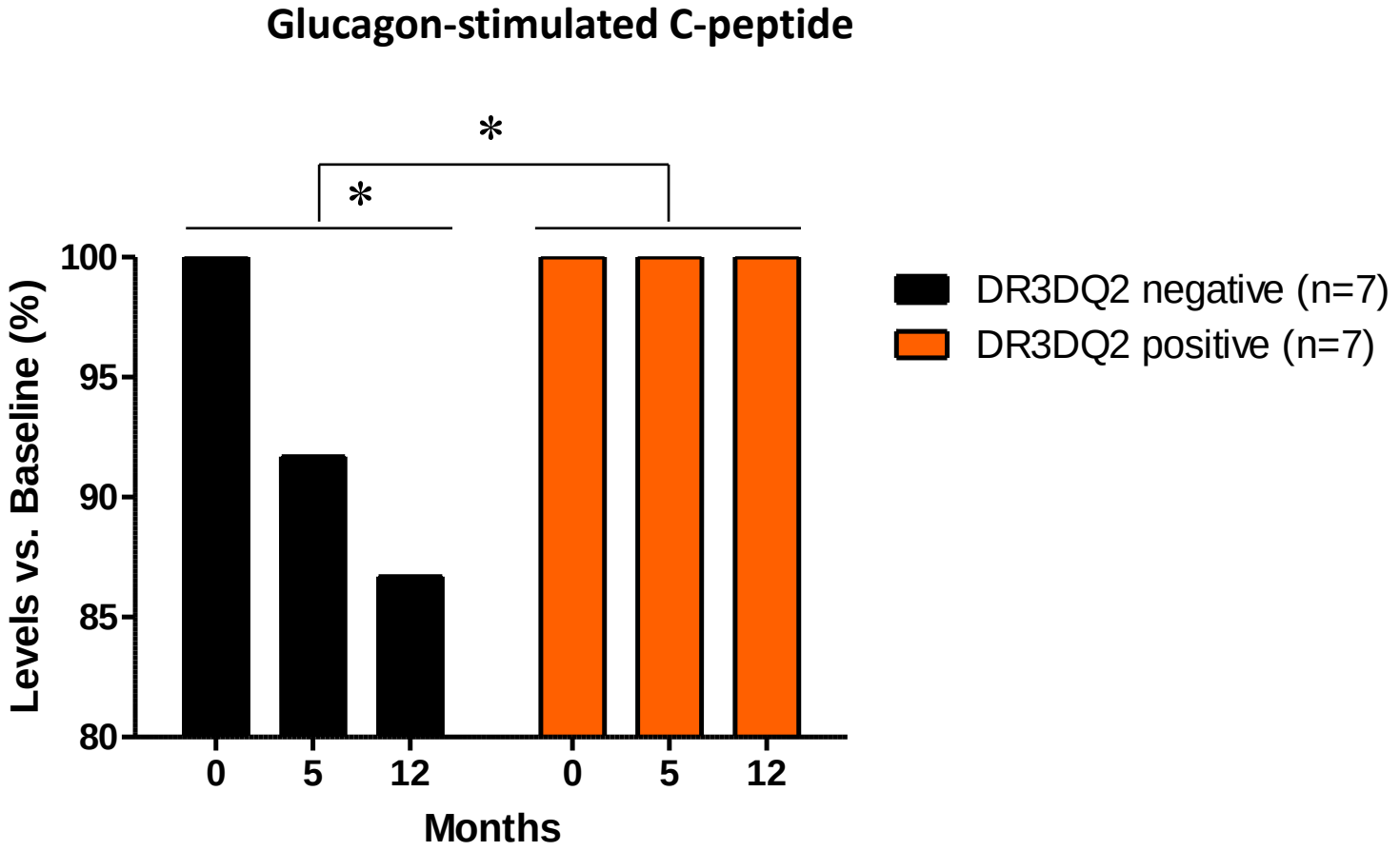


Hals IK, Fiskvik Fleiner H, Reimers N, Astor MC, Filipsson K, Ma Z, Grill V, *Björklund A. Investigating optimal β-cell-preserving treatment in latent autoimmune diabetes in adults: Results from a 21-month randomized trial*. Diabetes Obes Metab. 2019 Oct

DIAMYD MEDICAL

Glucagon-stimulated C-peptide levels unchanged at 12 months vs Baseline (0 months) in the HLA-DR3DQ2 positive subgroup

Phase 2 trial with Diamyd in up to 70 year-old LADA patients



*p< 0.03 for median 13.3% reduction at 12 months vs. Baseline (0 months) in the DR3DQ2 negative subgroup (n=7).

*p< 0.04 for difference between HLA subgroups in change at 12 months vs. Baseline (0 months).

Hals et al, A 1-year pilot study of intralymphatic injections of GAD-alum in individuals with latent autoimmune diabetes in adults (LADA) with signs of high immunity: No safety concerns and resemblance to juvenile type 1 diabetes, Diabetes, Obes Metab. 2023

DIAMYD MEDICAL

Conclusions

- Treatment with intralymphatic GAD is well tolerated in LADA individuals – no safety concerns
- GAD-induced immune responses appear compatible with those in studies with Type 1 Diabetes
- Results on C-peptide suggest an HLA-dependent beneficial effect akin to Type 1 Diabetes

Also see

- Latent Autoimmune Diabetes in Adults: Background, Safety and Feasibility of an Ongoing Pilot Study With Intra-Lymphatic Injections of GAD-Alum and Oral Vitamin D, Björklund et al, Front Endocrinol, 2022
- A 1-year pilot study of intralymphatic injections of GAD-alum in individuals with latent autoimmune diabetes in adults (LADA) with signs of high immunity: No safety concerns and resemblance to juvenile type 1 diabetes, Hals et al, Diabetes, Obes Metab. 2023
- Press release: Updated results from clinical trial with Diamyd® presented today at diabetes conference

DIAMYD MEDICAL

Type 1 Diabetes prevention (Stage 1 & 2)

DIAMYD MEDICAL

Press Release, November 7, 2023

Diamyd Medical partners with DiaUnion to recruit participants for Type 1 diabetes prevention trial

Diamyd Medical has entered into a collaboration agreement with DiaUnion, a center of excellence in type 1 diabetes, to identify participants for the DiaPrecise trial, an open-label trial evaluating the safety, feasibility and immune response of intralymphatic injections of Diamyd® in children at risk of developing type 1 diabetes who also carry the HLA DR3-DQ2 genotype. The DiaPrecise trial has been initated and is ongoing at the Department of Clinical Sciences at Lund University, Malmö, with Markus Lundgren M.D., PhD, as the Principal Investigator.

DIAMYD MEDICAL COORDINATES THE ASSET MILIEU

A T1D Forum to drive precision medicine, prevention and screening

Contact with T1D research community

Aim for a European-level contact network

Partnerships in developing AI algorithms

Discuss best practices for screening programs

Integration of data from different cohort studies

www.asset.healthcare

ASSET

ABOUT ASSET

The innovation milieu ASSET (AI for Sustainable Prevention of Autoimmunity in the Society – www.asset.healthcare) will develop and evaluate new algorithms based on AI to be able to assess the individual risk of developing Type 1 Diabetes (T1D), and the likelihood of responding to different treatments. Data from cohort studies such as TEDDY (The Environmental Determinants of Diabetes in the Young), from Diamyd Medical's clinical trials with Diamyd® and from sources such as the National Diabetes Registry will consitute the initial training dataset for the algorithm. T1D will form the pilot project for the program, but the goal is extend the functionality to other indications including other autoimmune diseases that are strongly linked to T1D such as celiac disease (gluten intolerance) and autoimmune thyroiditis (inflammatory disease of the thyroid gland). The prediction algorithm will be evaluated in clinical prevention trials where individuals at high risk for type 1 diabetes will be treated preventively with the diabetes vaccine Diamyd®. In parallel, ASSET will study organizational, economic, and legal prerequisites and consequences of applying the approach as a tool for precision health in the Swedish health care system. The project has a duration of five years and is financed via the Swedish innovation agency VINNOVA.

Mainly.AI

LUNDS UNIVERSITET

NDR NATIONELLA DIABETESREGISTRET

DIAMYD MEDICAL

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Leading Health Care

VINNOVA

ASSET publication on using AI for T1D screening published in Diabetologia and highlighted by EASD e-Learning

Home > Diabetologia > Article

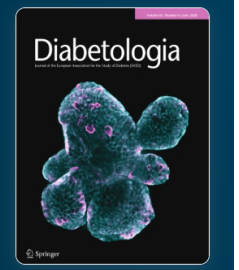
Assisting the implementation of screening for type 1 diabetes by using artificial intelligence on publicly available data

For Debate | Open access | Published: 14 February 2024

Volume 67, pages 985–994, (2024) Cite this article

Download PDF

You have full access to this open access article



Diabetologia

Aims and scope →

Submit manuscript →

DIAMYD MEDICAL

Manufacturing and Market Exclusivity of Diamyd®

Diamyd Medical is building a biomanufacturing plant for GMP commercial scale production of rhGAD65

Commercial-scale production of rhGAD65 planned to be ready for BLA/MAA and market entry

- 20,000 square feet facility in Umeå, Northern Sweden, comprising clean rooms, laboratory facilities and office space
- Manufacturing facility property fully acquired in 2022
- Full control over the manufacturing of recombinant GAD65
  - Independence from CDMOs, third parties
  - In control of costs and resource allocation
  - Potential beyond GAD manufacturing

DIAMYD MEDICAL

Full Control and Predictability of the Manufacturing Process

Diamyd Medical's Umeå facility uses the Baculovirus Expression Vector System (BEVS) in the complex manufacturing process of recombinant human GAD65 protein

Upstream process

Baculovirus expression system & insect cells

Downstream process

Clarification
Capture
Polish
Nanofiltration

Drug Product formulation

DIAMYD MEDICAL

DIAMYD® IP & MARKET EXCLUSIVITY

Core Intellectual Property

- **Substance of matter** in the US until **2032**
- **Intralymphatic administration** of Diamyd® in Europe, Japan, China, Australia, Russia and Canada, additional countries pending, expiry **2035.**
- Intralymphatic administration of additional betacell antigens (proinsulin, preproinsulin etc) approved in Australia, Israel, additional countries pending.
- **Precision medicine patent** based on HLA subgroups approved in Europe, Eurasia and South Korea, expiry **2035**, additional countries pending.

Regulatory exclusivity

- US BLA approval provides **12 years exclusivity**
- US orphan designation provides **7 years exclusivity** from approval
- European approval provides **10 years of exclusivity**
- US Fast Track designation → potential for **priority review**, **rolling review**

DIAMYD MEDICAL

Remygen®

Modified Release GABA

Primary Indication
Type 1 diabetes

Label expansion
LADA, Insulin-deficient type 2 diabetes

Mechanism of Action
Activate GABA-receptors in the pancreas

Clinical Effect
- *Regenerate endogenous insulin production, reduce short- and long-term complications*
- *Prevention of hypoglycemia*

Mode of Administration
Oral

Development status
Phase Ib/IIa

Licensing Status
Global rights available

DIAMYD MEDICAL

Clinical results with attractive path to market for Remygen®

- Phase Ib/IIa first in man trial
  - ReGenerate-1 at the University of Uppsala where Remygen® (proprietary formulation of GABA) alone and in combination with low-dose alprazolam (GABA receptor modulator to enhance effect, see next slide) evaluated in long-standing type 1 diabetes patients
  - Clinical effects (Phase Ib dose-escalation) shown on **preventing hypoglycemia by correcting the counter regulatory hormone response** and **increasing time-in-range** in long-term type 1 diabetes (published), potential trend for acute effect of Remygen shown in Phase IIa (further data analyses ongoing).
  - Long-term safety of all doses of GABA as well as combination with low-dose Alprazolam
- Clinical effects of GABA (non-proprietary formulation) shown on **decreasing glucagon secretion** in recent-onset type 1 diabetes and immunological effects shown on altering Th1 response
- Preclinical effects on insulin secretion, glucagon secretion and beta cell regeneration
- Endogenous substance with very good safety profile

DIAMYD MEDICAL

biomedicines

MDPI

Article

GABA and Combined GABA with GAD65-Alum Treatment Alters Th1 Cytokine Responses of PBMCs from Children with Recent-Onset Type 1 Diabetes

Katie E. Heath [1,†], Joseph M. Feduska [1,†], Jared P. Taylor [1], Julie A. Houp [2], Davide Botta [1], Frances E. Lund [1], Gail J. Mick [3], Gerald McGwin, Jr. [4], Kenneth L. McCormick [3] and Hubert M. Tse [5,*]

Open access Original research

BMJ Open Diabetes Research & Care

GABA induces a hormonal counter-regulatory response in subjects with long-standing type 1 diabetes

Daniel Espes ,[1,2] Hanna Liljebäck,[3,4] Henrik Hill,[5] Andris Elksnis,[3] José Caballero-Corbalan,[4] Per-Ola Carlsson[3,4]

nature communications

Article

https://doi.org/10.1038/s41467-022-35544-3

A randomized trial of oral gamma aminobutyric acid (GABA) or the combination of GABA with glutamic acid decarboxylase (GAD) on pancreatic islet endocrine function in children with newly diagnosed type 1 diabetes

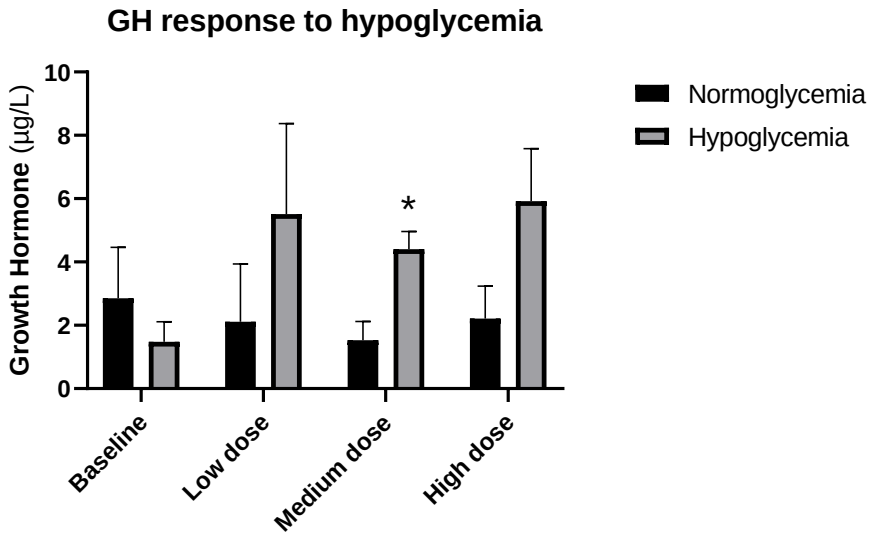
Received: 27 October 2021

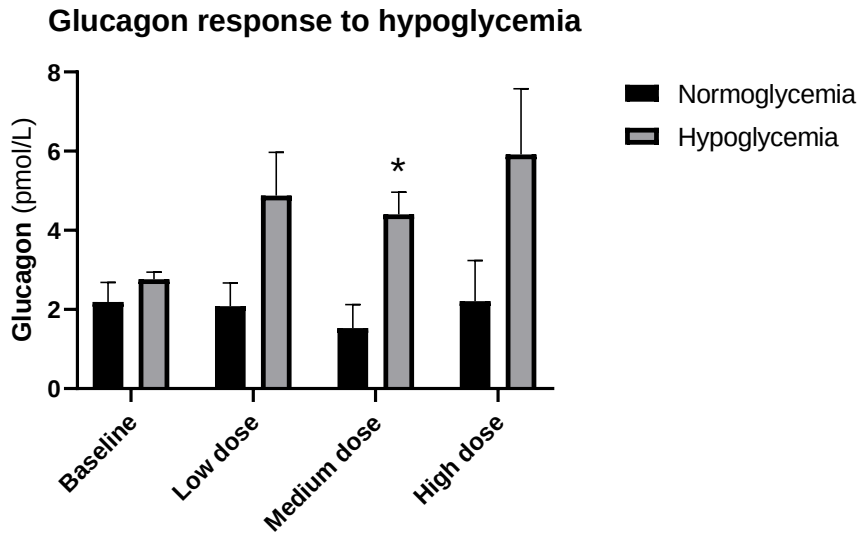
Accepted: 6 December 2022

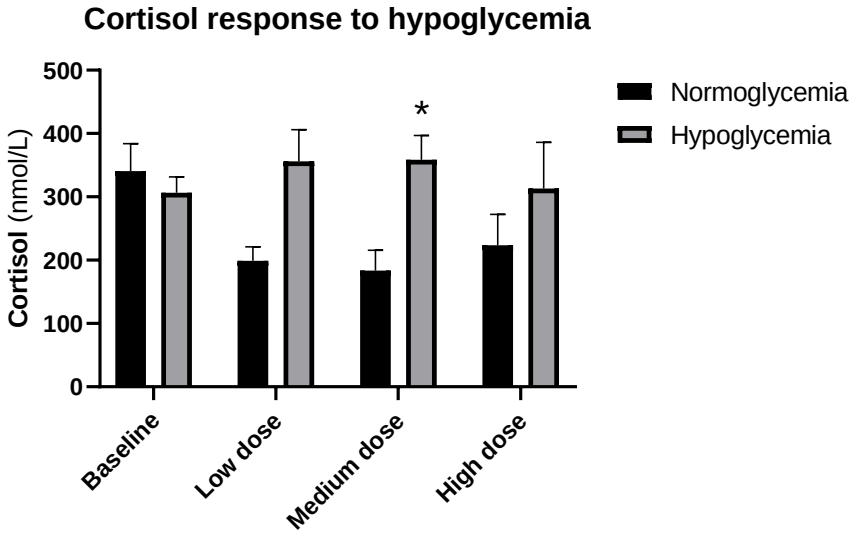
Published online: 24 December 2022

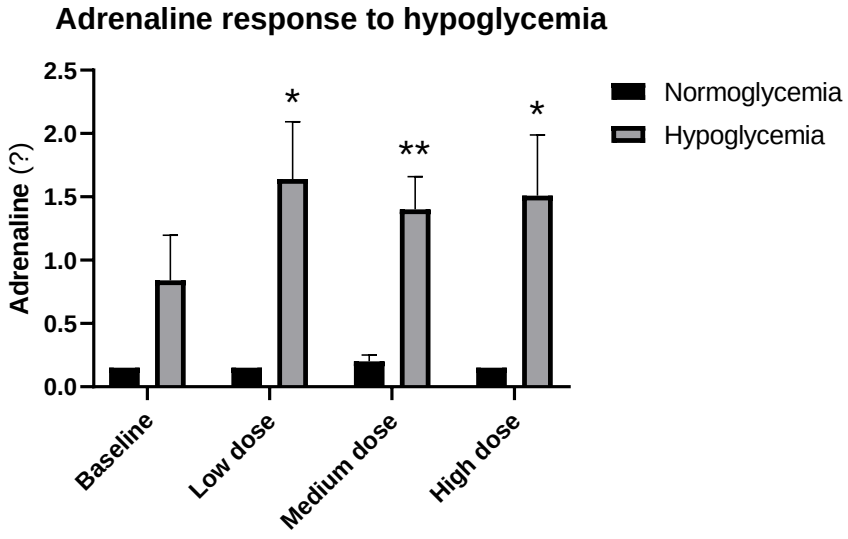
Alexandra Martin[1,4], Gail J. Mick[1,4], Heather M. Choat[1], Alison A. Lunsford[1], Hubert M. Tse[2], Gerald G. McGwin Jr.[3] & Kenneth L. McCormick[1]

GABA TREATMENT IMPROVES THE HORMONAL RESPONSE TO HYPOGLYCEMIA









Comparisions between noro- and hypoglycemia for the respective group using a multiple T-test with p-values corrected for multiple testing using the Holm-Sidak method.
* denotes $p<0.05$, ** <0.01
Values are given as mean±SEM

Data based on ReGenerate-1 clinical trial. First presented by professor Per-Ola Carlsson om the Word Diabetes Day 2020

DIAMYD MEDICAL

REMYGEN® MARKET EXCLUSIVITY AND MANUFACTURING

Core Intellectual Property

- **Exclusive license from UCLA** on treating diabetes and other inflammatory diseases with GABA
- **Formulation patent** application (Remygen®). Application in national phase.
- **Exclusive license from UCLA** on GABA in combination with GABA receptor modulators to enhance the regenerative and immunomodulatry effect. Application in national phase.

Regulatory exclusivity

- 505(b)(2) regulatory pathway in the US provides potentially faster time to market at reduced cost

Manufacturing

- GMP drug substance (GABA) and drug product (Remygen®) manufacturing in place

DIAMYD MEDICAL

Management

Dr. Ulf Hannelius, PhD, MBA
President & Chief Executive Officer

Martina Widman, MSc
Chief Operating Officer

Anna Styrud, BSc
Chief Financial Officer

Anton Lindqvist, MSc
Chief Scientific Officer

Dr. Maja Johansson, PhD
Chief Operating Officer – Manufacturing Site

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University of London

Professor Dr. Åke Lernmark, MD, PhD
Lund University

Professor Dr. Daniel Kaufman, PhD
UCLA School of Medicine

DIAMYD MEDICAL

Top worldwide experts

Covering the areas of clinical practice and scientific excellence in type 1 diabetes and

Prof. Johnny Ludvigsson

Professor of Pediatrics. First in the world to use immune intervention in children and teenagers with newly diagnosed T1D, and in collaboration with others

64kD was found. An alum-formulation of GAD was developed (Diamyd®), used as a treatment in an effort to deviate the immune system and create tolerance.

Prof. David Leslie

Professor of Diabetes and Autoimmunity. Professor Leslie has been Director of the British Diabetic Twin Study since 1982, the world's largest twin study of its type and Principal Investigator of the European Action LADA consortium. By studying twins, Professor Leslie has been able to show the possibilities for predicting and preventing autoimmune diabetes.

Prof. Åke Lernmark

Professor in Experimental Diabetes Research, Professor Lernmark has focused his research on diabetes and at an early stage identified the antigen that later proved to be GAD. He and his colleagues were the first to clone GAD65 from human islets using biochemical methods and was thus the first to define autoantibodies against GAD65 in patients with type 1 diabetes.

Prof. Daniel Kaufman

Professor Kaufman's research is focused on studies in the field of autoimmunity, particularly type 1 diabetes (T1D) and understanding the disease mechanisms in order to develop novel therapeutics in mouse models that could potentially be translated to clinical use. Using preclinical models, Dr. Kaufman’s lab helped to develop some of the GAD and GABA-based diagnostics and therapeutics for T1D that are in clinical use or are being tested in clinical trials.

Prof. Mark A. Atkinson

Professor of Diabetes Research, Department of Pathology, Immunology and Laboratory Medicine, University of Florida, USA. American Diabetes Association Eminent Scholar for Diabetes Research. Director, UF Diabetes Institute, University of Florida. Independent of the Company and its principal owners.

Diamyd Medical Board member.

DIAMYD MEDICAL

DIAMYD MEDICAL

- Swedish clinical phase pharmaceutical company, founded 1994
- NASDAQ First North Growth Market, ticker DMYD B

FINANCES

- Market Cap Oct 8, 2024 ~ MSEK 1,500
- Cash Aug 31, 2024: MSEK 132 (additional MSEK 48 + 17.5 in warrants and milestone payments)

INDICATIONS

- Diabetes
- Autoimmunity

PRODUCT CANDIDATES

- Diamyd® (Phase III)
- Remygen® (Phase Ib/IIa)

INVESTMENTS

- NextCell Pharma (Stockholm, Sweden)
- MainlyAI (Stockholm, Sweden)

Diamyd Medical

www.diamyd.com

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