Intercepting autoimmunity to prevent disease

proventionbio

Provention Bio

Forward looking statements

This presentation contains forward-looking statements including, but not limited to, those relating to the Company's product development, clinical studies, clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statements that are predictive in nature. "Forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 are statements that are not historical facts and involve a number of risks and uncertainties, which may cause actual results to be materially different from any future results expressed or implied in the forward-looking statements. These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential," "predict," "project," "should," "would" and similar expressions and the negatives of those terms.

Forward-looking statements are based on the Company's current expectations and assumptions. Forward-looking statements are subject to a number of risks, uncertainties and other factors, many of which are beyond the Company's control, including, but not limited to, our lack of operating history; our ability to satisfy our capital needs; our dependence on our product candidates, which are still in preclinical or various stages of clinical development; our dependence on third-parties to manufacture our product candidates; our reliance on third-party vendors, such as contract research organizations and contract manufacturing organizations; the uncertainties inherent in clinical testing; our ability to complete required clinical trials for our product candidates and obtain approval from regulatory authorities for our product candidates; our ability to protect our intellectual property; the loss of any executive officers or key personnel and the other factors listed under "Risk Factors" in our annual report on Form 10-K for the year ended December 31, 2018 and any subsequent filings with the Securities and Exchange Commission (SEC).

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Intercepting autoimmunity to prevent disease

Strategic focus on autoimmunity with emphasis on immuno-endocrinology

- Focused on chronic autoimmune indications with compelling biological and commercial rationale
- Lead program in autoimmune, Type 1 diabetes (T1D)

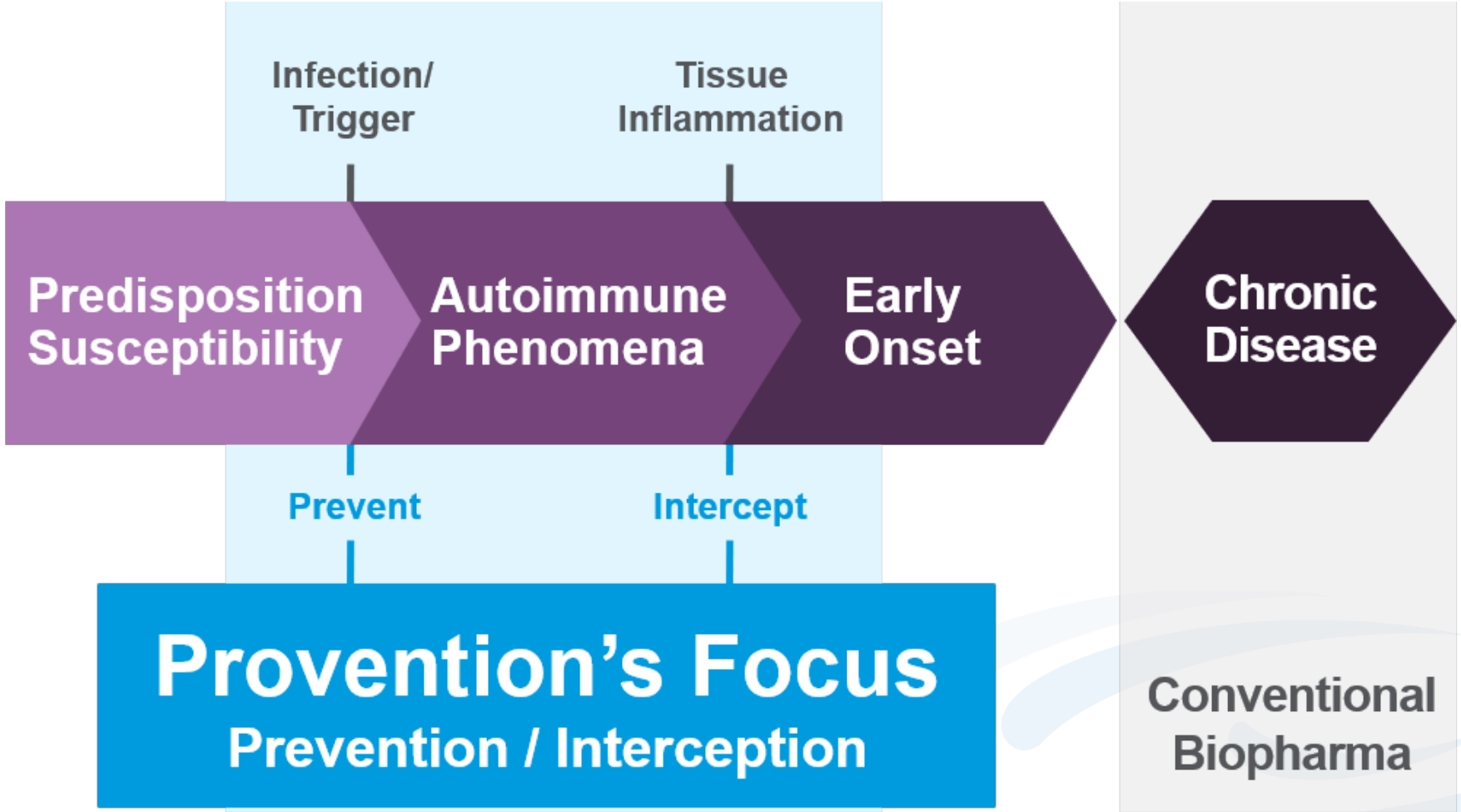
Significant investment upside across all 4 programs

- PRV-031 (teplizumab)
  - For the delay or prevention of T1D
    - Expect BLA filing in Q4 2020; potential approval in mid-2021
    - Commercial opportunity >$1B in the US alone for the at-risk T1D indication
  - Multiple expansion opportunities, including in newly-diagnosed T1D
- Advancing three clinical-stage programs in the near term:
    - PRV-3279 a bispecific targeting B-cell driven disease with multi-indication potential
    - PRV-101 a vaccine for the prevention of coxsackie virus and potentially T1D and celiac
    - PRV-015 a mAb for non-responsive celiac disease

Strong financial position

- $95.1 million of cash at September 30, 2019

Treating disease chronically is not ideal…



Pipeline

Autoimmune indication agnostic pursuit targeting upstream pathways in T and B cell biology

Focus	Indication	Preclinical	Phase I	Phase II	Phase III	Regulatory	Next Expected Milestone
Type 1 Diabetes (T1D) Autoimmunity	At-Risk	PRV-031 (Teplizumab)					BLA filing in Q4 2020
	Newly Diagnosed	PRV-031 (Teplizumab)					Complete PROTECT enrollment Q4 2020
	Prevention	PRV-101					Phase 1 first-in-human data in 2021
B-Cell Autoimmunity Checkpoint	SLE	PRV-3279					Top-line results of Phase 1b in Q1 2020
	Prevention of immunogenicity	PRV-3279					Preclinical data
GI Autoimmunity	Celiac Disease	PRV-015					Initiate Phase 2b trial Q2 2020

Program partners

AMGEN®

T1D: high unmet need and disease burden

Orphan Genetically Predisposed Autoimmune Disease

- ~40,000 new diagnoses per year in US
- ~50% of newly diagnosed patients present with a critical, life-threatening condition called diabetic keto acidosis (DKA)
- ~60% of cases associated with coxsackievirus B infection
- ~300k people at risk in the US of progressing to T1D

Unmet Need

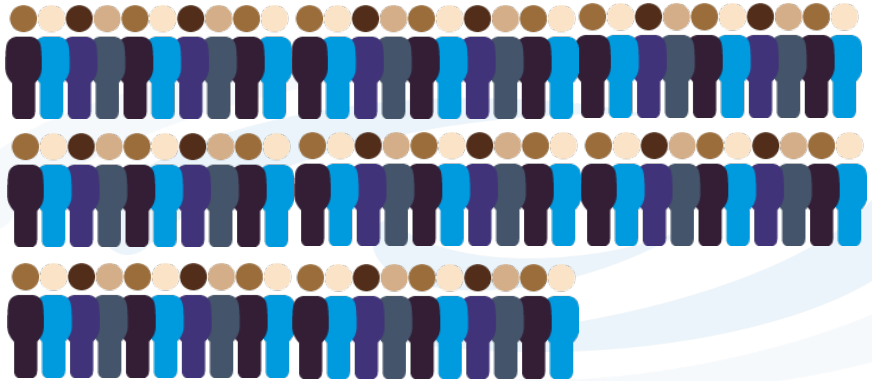
- Currently no preventive or disease-modifying treatments
- No new therapies since insulin (1922)
- >75% of T1Ds are poorly controlled (HBA1c > 7%), leading to cardiovascular disease, kidney disease, retinopathy and metabolic syndrome
- Life expectancy ~16 years shorter if diagnosed before age 10

New Onset 40,000
Yearly US T1D incidence

= 20,000 People

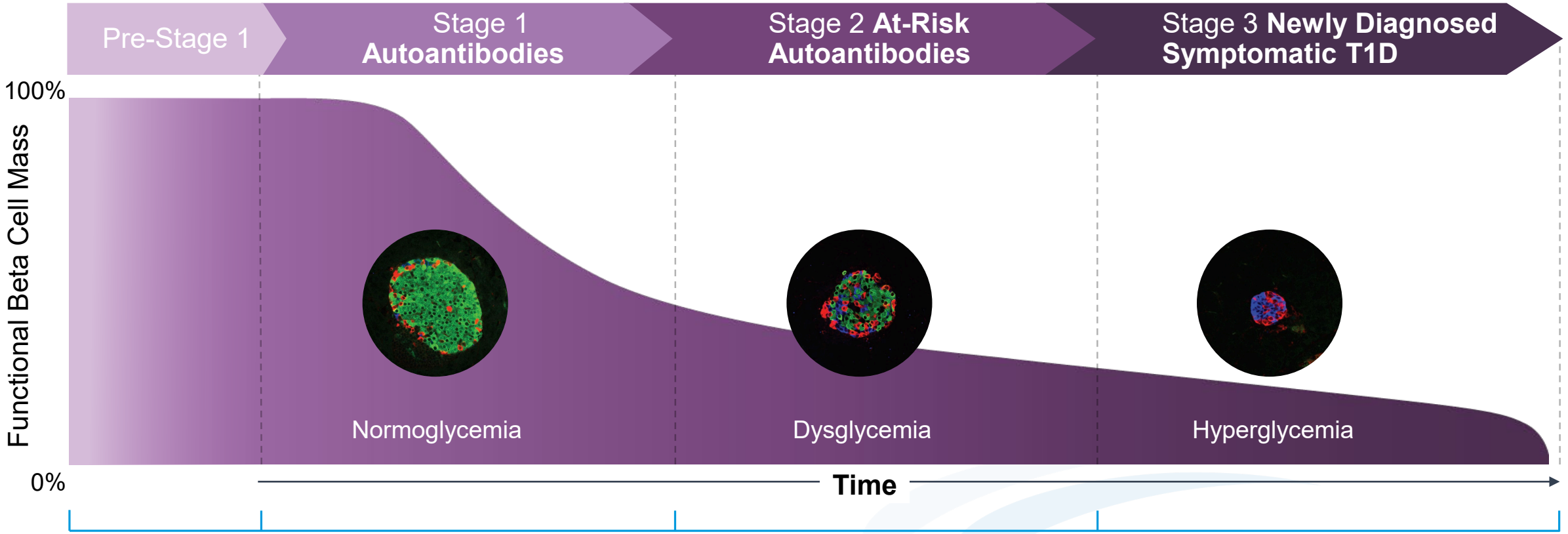
At Risk prevalence of at least 300,000 in the US (Stage 1 and 2 T1D)

Prevalence 1.6 million
Living with T1D in US



T1D continuum leads to destruction of β cells

Natural history of β cell loss and T1D onset



Staging Presymptomatic Type 1 Diabetes. Insel et. al. Diabetes Care 2015;38:1964–1974 | DOI: 10.2337/dc15-1419

PRV-031 (teplizumab): Intercepting T1D

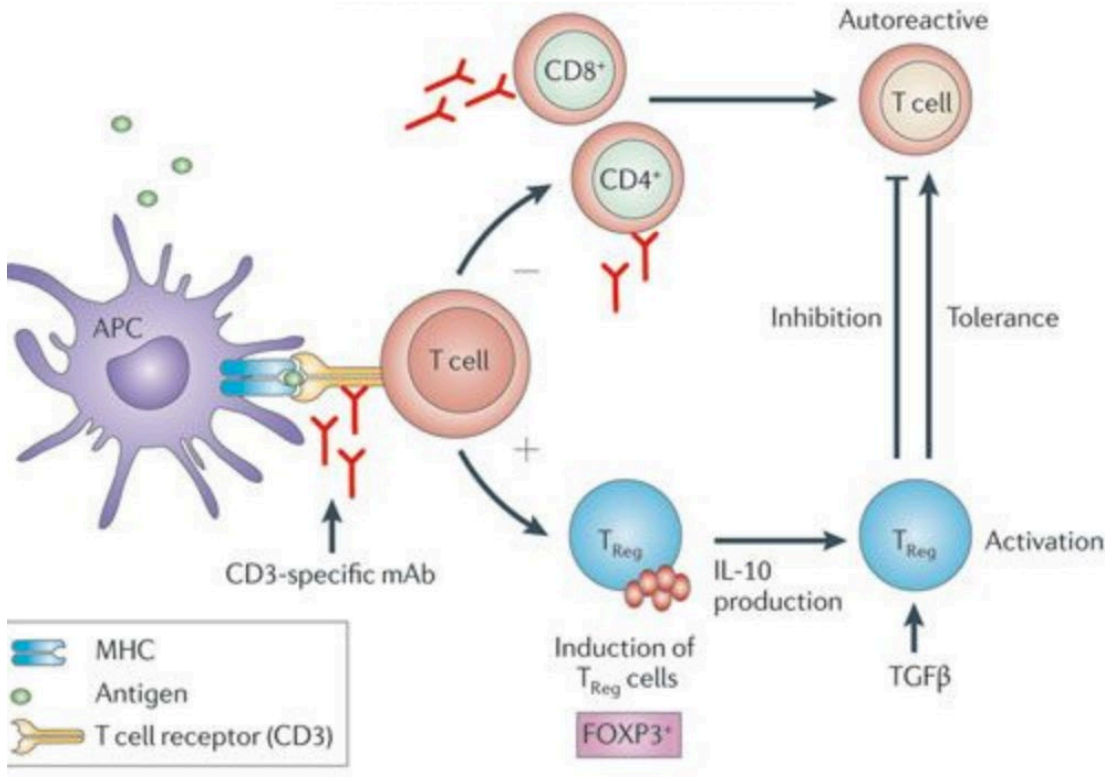
Mechanism of Action

- Humanized monoclonal antibody
- Binds to T-cell co-receptor CD3, acting as partial agonist
- Administered as a single course of 12- or 14-day outpatient treatment (~30-minute IV infusion with no steroid premedication required)

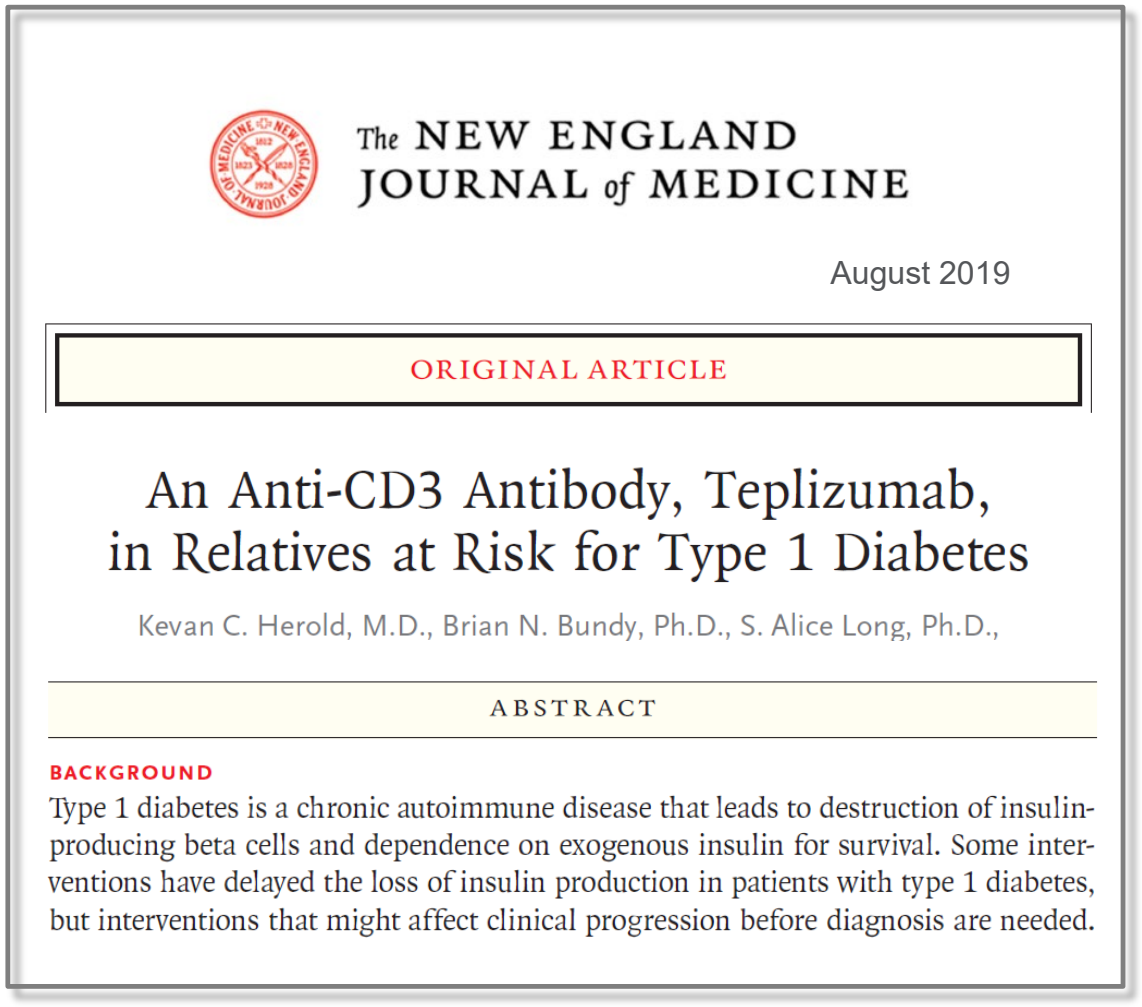
Supporting Clinical Data

- >800 patients dosed across multiple clinical studies
- Consistent C-peptide benefit and reduction in insulin use in newly diagnosed T1D patients
- “At-Risk” results: significantly delayed T1D onset

Eliminating Autoreactive T-cells While Sparing Regulatory T-cells



At-Risk study in T1D



The NEW ENGLAND JOURNAL of MEDICINE

August 2019

ORIGINAL ARTICLE

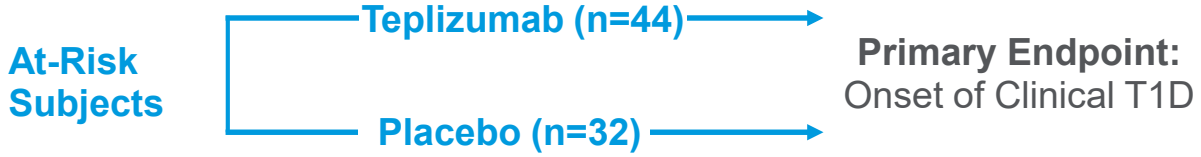
An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes

Kevan C. Herold, M.D., Brian N. Bundy, Ph.D., S. Alice Long, Ph.D.,

ABSTRACT

BACKGROUND

Type 1 diabetes is a chronic autoimmune disease that leads to destruction of insulin-producing beta cells and dependence on exogenous insulin for survival. Some interventions have delayed the loss of insulin production in patients with type 1 diabetes, but interventions that might affect clinical progression before diagnosis are needed.



Primary Endpoint

- Time to development of T1D from randomization after single 14-day course of teplizumab by IV infusion

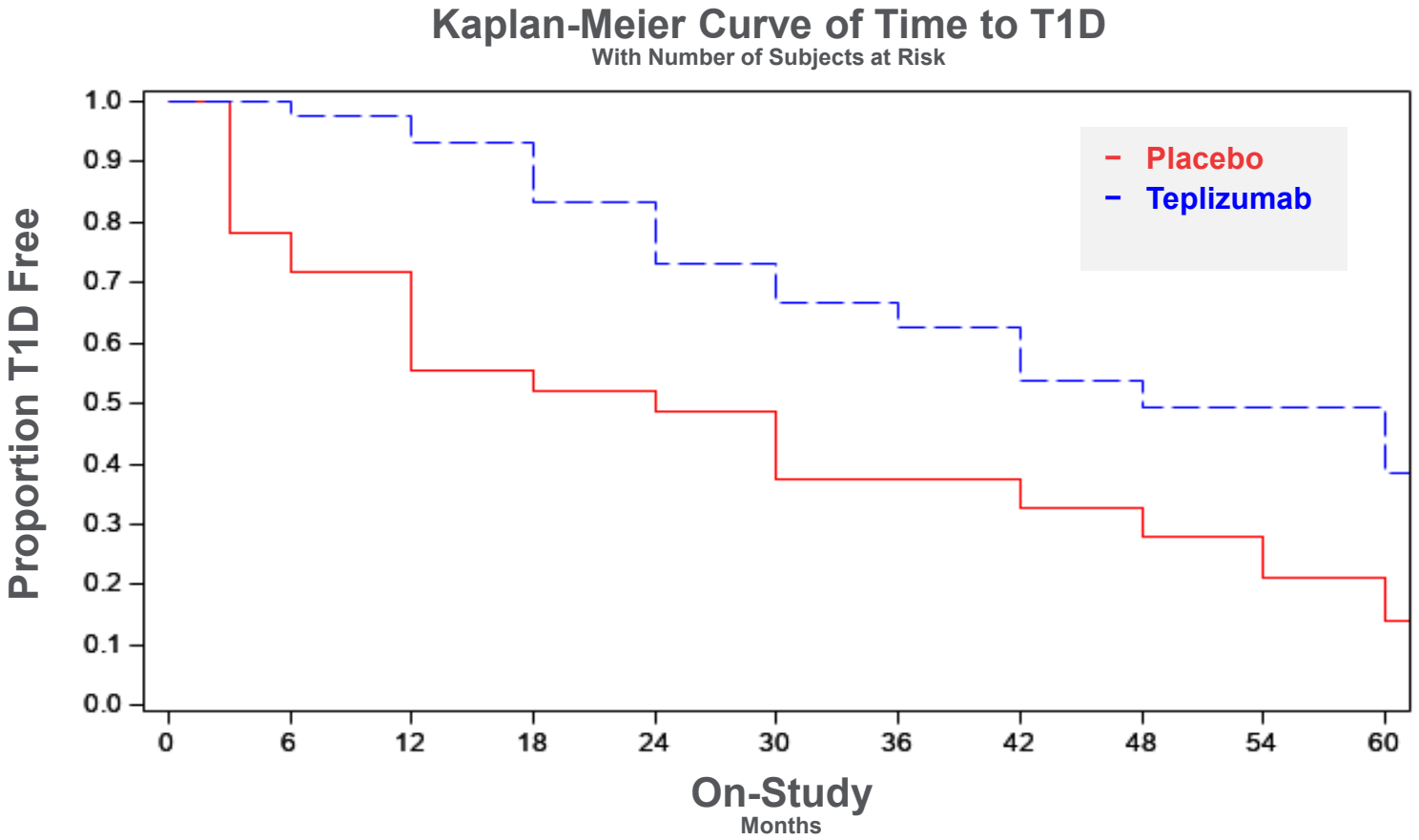
Population

- ≥ 8 years old, relative of a patient with T1D
- Abnormal glucose tolerance
- ≥ 2 T1D-related autoantibodies

Conducted by TrialNet

- Funded by the NIH and JDRF

At-Risk study shows delay of T1D by at least 2 years



Median Time to T1D Diagnosis

Teplizumab:	**48.4 months**
Placebo:	**24.4 months**

Overall hazard ratio 0.412
(95% CI: 0.216, 0.783)
(p=0.006, two-sided, Cox model)

	Teplizumab (N=44)	**Placebo** (N=32)
Freedom from T1D	**25/44** (57%)	**9/32** (28%)
Annualized Rate of T1D	**14.9%**	**35.9%**

- **Single 14-day course of PRV-031 significantly delayed the clinical onset of T1D by 24 months (p=0.006)**
- **Decreased annualized rate of T1D by ~60%**
- **Some subjects yet to develop diabetes >7.5 years from start of treatment**

At-Risk: favorable safety profile

Adverse Effect Category	PRV-031		Placebo	
Events occurring in ≥5% of subjects:	**Number of Events**	**Number of Subjects (%)**	**Number of Events**	**Number of Subjects (%)**
Blood/Bone Marrow	45	33 (75.0)	2	2 (6.2)
Dermatology/Skin	17	16 (36.4)	1	1 (3.1)
Pain	11	5 (11.4)	5	3 (9.4)
Infection	8	5 (11.4)	5	3 (9.4)
Gastrointestinal	5	4 (9.1)	3	3 (9.4)
Metabolic/Laboratory	7	4 (9.1)	2	2 (6.2)
Pulmonary/Upper Respiratory	6	4 (9.1)	0	0 (0)
Endocrine	0	0 (0)	2	2 (6.2)
Total Events and Subjects	**112**	**44 (100)**	**23**	**32 (100)**

Expected finding based on drug/mechanism, including transient white blood cell margination and self-limited mild rash

No reports of increased infection risk to date.

Historical data set included for regulatory submission

At-Risk trial data will be supported by efficacy and data set from >800 patients

Study	Phase 3: Protégé*	Protégé Subgroup	Phase 2: Study 1	Phase 2: AbATE	Phase 2: Delay**
Number of Subjects	**513**	**89**	**40**	**77**	**58**
T1D diagnosis	< 12 weeks	< 12 weeks	< 6 weeks	< 8 weeks	4 - 12 months
Subject population	Age 8-35 years Mean 18.4 years	Age 8-17 years and baseline C-peptide > 0.2 pmol/mL	Age 8-30 years Mean 13 years	Age 8-30 years Mean 13 years	Age 8-30 years Mean 12.6 years
Difference in C-peptide	24%	43%	145%	92%	27%
P-value	0.027	0.026	0.02	0.002	0.03

Consistent C-peptide benefit indicating preservation of beta cells

* Full 9.0 mg/m^2/course 14-Day regimen was explored in 205 treated patients and 98 placebos
**Delay study based on 12-month time-point. All other studies based on 24 month time-points

Regulatory Strategy

Based on November 2019 Meeting with FDA, We Plan to Complete a Rolling BLA Submission in 2020

- Expect to submit clinical and non-clinical modules in mid-2020
- Expect to submit CMC module in Q4 (critical path is manufacturing of comparable batches)

Received Breakthrough Therapy Designation (August 2019) and PRIME Designation (October 2019)

- For the prevention or delay of clinical T1D in at-risk individuals
- Provides for greater dialog with FDA and EMA
- Increases likelihood of Priority Review by FDA and Accelerated Assessment by EMA

Timelines to Potential Approval in At-Risk Indication

- US/FDA: potential approval in 2021 (assumes priority review: 8-month review vs. traditional 12-month review)
- EU/EMA: potential approval in 2022; meeting targeted for Q1 2020

Will file for Newly Diagnosed Indication in 2022

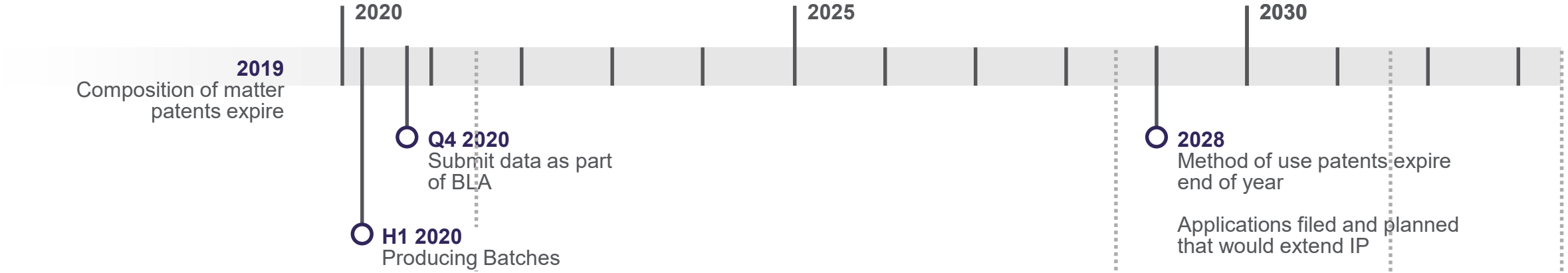
- Expect to complete PROTECT Phase 3 study enrollment in Q4 2020; top-line data in 2022

Teplizumab manufacturing on track

Lilly → AGC

Teplizumab manufacturing process has been transferred to AGC (prior manufacturing conducted by Eli Lilly)

Current production scale is sufficient for launch
- Teplizumab is highly potent and requires low volume for administration



Regulatory exclusivities provide additional market exclusivity beyond core IP

- **US BLA approval provides 12 years of protection**
- **US Orphan indication provides 7 years of protection**
- **EU approval allows for 10 years of protection**

Teplizumab Commercialization and Patient Screening

"At-Risk" study results and the prospect of T1D disease-modifying therapies will greatly increase screening and facilitate teplizumab's commercialization . . .

Current Screening

- Standard T1D blood tests available
- Over 1.5 million people screened to date
- Diagnosing patients at earlier stages of disease can help reduce disease morbidity[1]
  - DKA reduced from ~50% down to ~15%[2]
- Identification rates for 2 auto-antibodies:
  - Family history ~1:100[3]
  - No family history ~1:1,000[4]

Future Screening

- *We believe an approved treatment to delay or prevent T1D will catalyze the awareness and rationale for broader based population screening*
- *Initial focus is on screening of familial direct relatives of T1D patients with parallel efforts on modifying guidelines for T1D management*
- *Screening will expand into the general population facilitated by the availability of lower cost and more accessible tests*

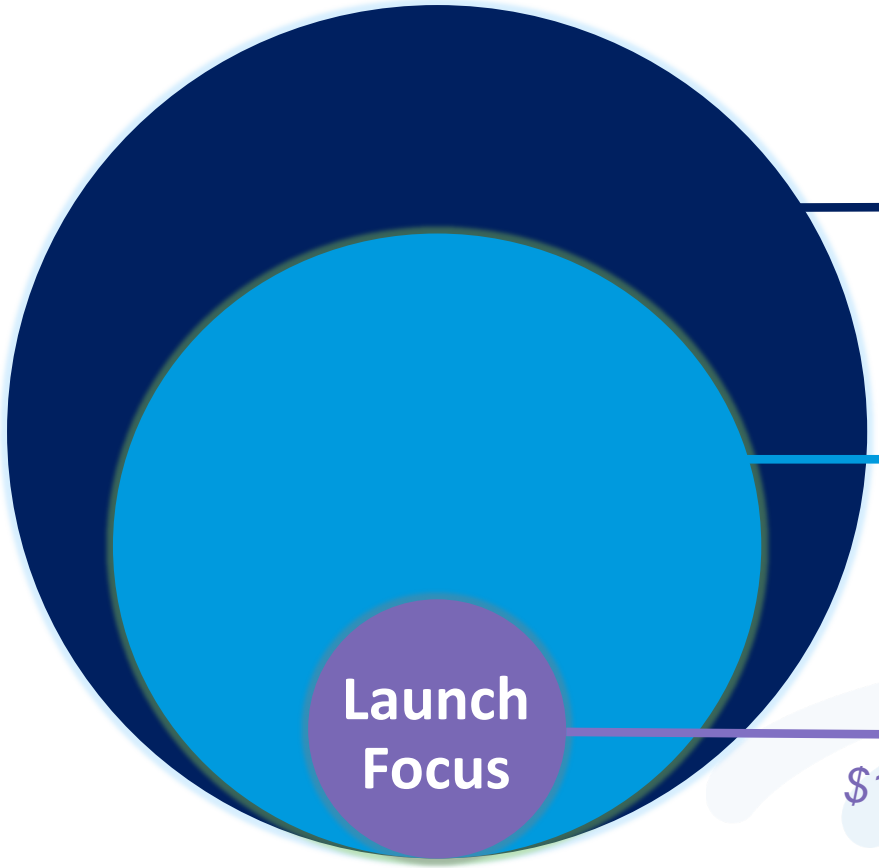
1. Ziegler et al. Yield of Public Health Screening of Children for Islet Autoantibodies in Bavaria Germany; JAMA. 2020;323(4):339-351. doi:10.1001/jama.2019.21565
2. Rewers et al, ASK poster at EASD 2019; 3. Rewers et al ASK poster at EASD 2018; 4. Bonifacio et al, PLOS Medicine April 3, 2018

US Commercial Opportunity for At-Risk Indication

Up to 2,300,000 patients may be at-risk for T1D globally

Future broader population screening will expand market significantly beyond Familial Direct Relatives

Label expansion initiatives will include multiple courses of treatment



Estimated US Patient Prevalence

2 or more autoantibodies
300,000

2 or more autoantibodies and dysglycemia
200,000

Familial Direct Relatives of T1D patients
30,000

$1B+ yearly revenue opportunity in the US
EU patient estimates similar to that of US

Laying the groundwork for successful commercialization

Near-Term Focus

- US commercial planning for at-risk indication
- Disease awareness
- HCP and KOL engagement
- Patient advocacy group partnerships
- Screening preparations

Mid-Term Focus

- EU commercialization with a partner
- Newly diagnosed indication launch

Longer Range

- Market expansion with broader population screening
- Addition of age groups and multiple courses of treatment for both at-risk and newly diagnosed indications

Significant upside expected from ex-US geographies, label expansion, screening initiatives

PRV-031 (teplizumab)

T1D lifecycle and other potential indications

T1D Lifecycle

Repeat Dosing

- At-Risk
- Newly Diagnosed

Age Expansion

- At-Risk (ages 2-8)
- Newly Diagnosed (ages 2-8 and >18)

Combinations in T1D

- Antigens
- Metabolic drugs (GLP-1 agonist)
- Immune modulator (B cell inhibitor, PRV-3279, anti-TNF)
- Beta cell transplant

Subcutaneous Formulation

Other Indications

GI Immunology

- Crohn's disease
- Celiac disease
- Autoimmune hepatitis

Rheumatology

- Psoriatic arthritis
- Rheumatoid arthritis

PROTECT Phase 3 in newly diagnosed T1D

Objective

- Preserve beta cell function in T1D patients that are most responsive to teplizumab

Primary Endpoint

- Difference in C-peptide at 18 months (detect a 40% difference with 90% power)

Secondary Endpoints

- Insulin use
- HbA1c
- Hypoglycemic episodes
- Safety

Status

- Expect to complete enrollment in Q4 2020
- Data expected in 2022

Trial Design

300 participants

Randomized 2:1 (teplizumab:placebo)

Age range: 8–17 years old

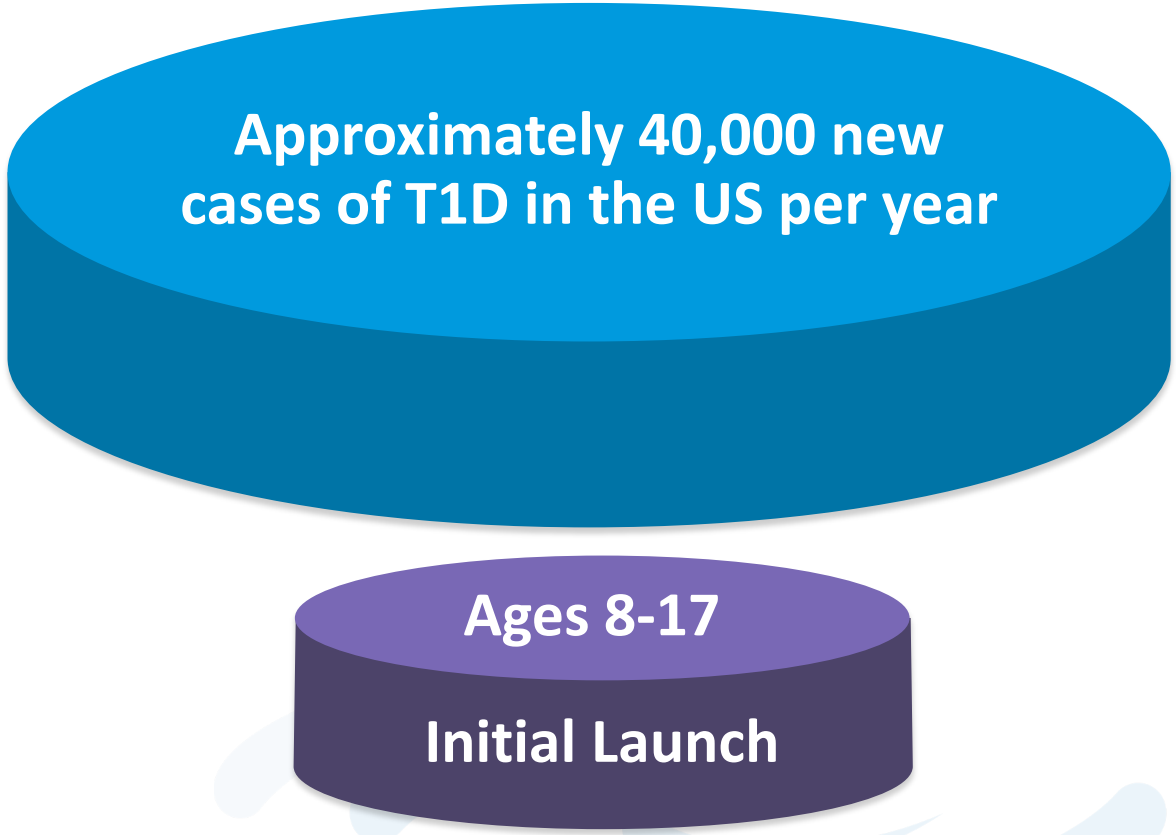
Newly diagnosed: within 6 weeks of T1D diagnosis

- **Baseline C-peptide >0.2 pmol/mL**
- **T1D-related autoantibodies**

US Commercial Opportunity for Newly Diagnosed Indication

Newly diagnosed type 1 diabetes patients will be more easily identifiable via outreach to pediatric and adult endocrinologists

Future age groups will include 2-7 year old and 18+ year old patients



Vaccine to prevent T1D and celiac disease

Vaccinating Against Coxsackievirus B (CVB)

- PRV-101 is a polyvalent inactivated vaccine
- Designed to prevent acute CVB infection, as well as a subset of T1D and celiac disease

Rationale

- CVB is a common, potentially serious infection
- CVB found in the pancreas of ~60% of patients with T1D and in the gut of ~20% of patients with celiac disease
- Infects and damages insulin-producing cells and gut lining cells, triggering an activated T-cell immune response
- In certain genetic backgrounds, response becomes autoimmune → T1D and/or celiac disease
- 50% reduction in T1D in offspring of mothers with immunity to CVB during pregnancy

Status

- Expect to file IND and initiate Phase 1 trial in H2 2020
- First-in-human data expected in 2021

The Big Idea

CVB vaccine has the potential to prevent acute coxsackie infection and the potential to prevent up to ~50% of T1D and ~20% of celiac disease.

CVB is the only persistent infection associated with development of T1D and celiac autoimmunity (TEDDY study of >400,000 children screened)

Phase 1 first-in-human study

Objective

- Safety, tolerability and immunogenicity of PRV-101 in adult healthy volunteers

Primary Endpoint

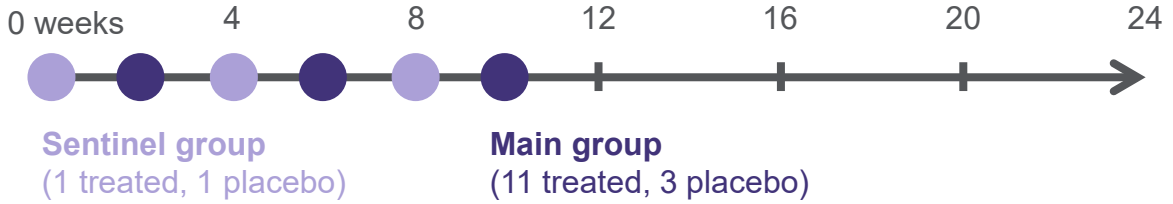
- Safety

Secondary Endpoints

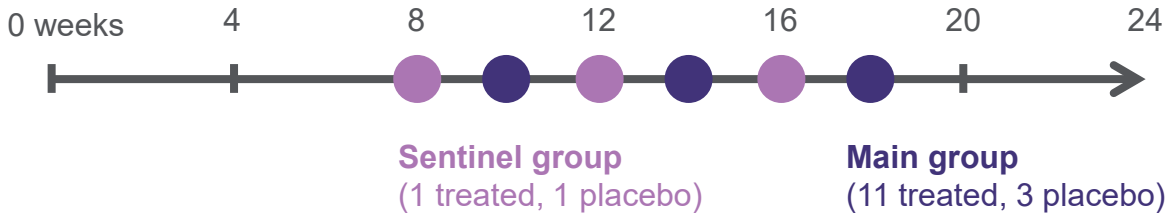
- Immune monitoring (CVB serotype seroconversion, neutralizing antibodies)

Trial Design and Structure

Cohort 1



Cohort 2



Randomized, double-blind, placebo-controlled, dose-escalation study to evaluate the safety, tolerability and immunogenicity of PRV-101 in healthy volunteers

Two dose levels, each with a sentinel group. Three vaccine administrations, every four weeks

PRV-3279 B-Cell Autoimmunity Checkpoint Inducer

Bispecific DART program

Unique MOA

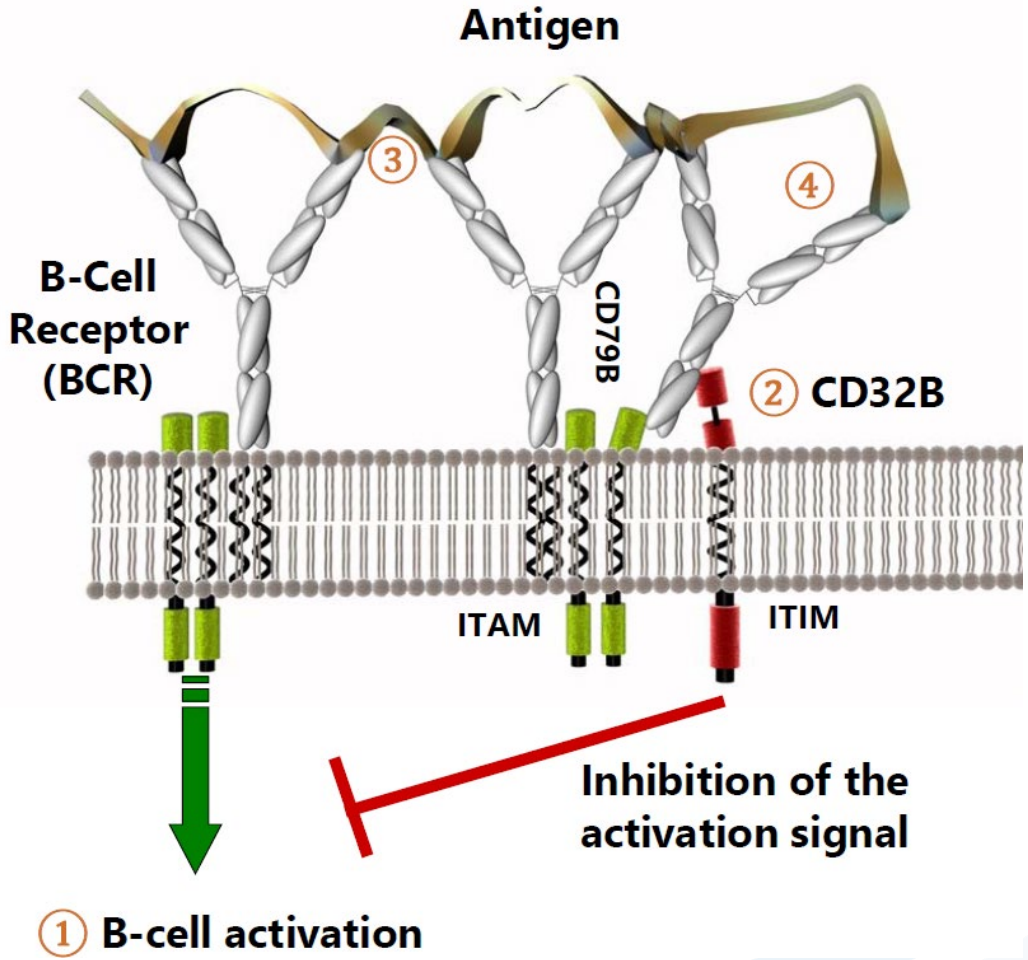
- Humanized, bi-specific scaffold (DART®) targeting both CD32B and CD79B
- Triggers inhibition of B cell function, suppression of auto-antibody production, and CD40 expression
- Boosts negative feedback loop regulating B cells, without causing B cell or platelet depletion

Established Proof-of-Mechanism

- Well tolerated in Phase 1a study
- Inhibition of the production of antibodies to Hepatitis A vaccination in previously unvaccinated individuals
- Durable effect: 1-month B cell inhibition after single dose

Multiple Potential Applications

- Intercept autoimmune diseases, such as lupus
- Prevent immunogenicity of a variety of therapeutic proteins and gene therapy vectors



Phase 1b/2a PREVAIL study design

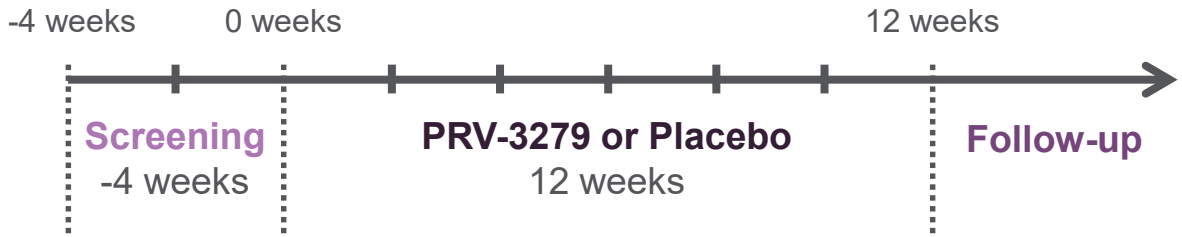
PREVAIL Part 1 - Design

- Multiple-Ascending Dose (MAD) Phase 1b study in adult healthy volunteers
- Randomized, double-blind, placebo-controlled

PREVAIL Part 1 - Results

- Expect top-line results Q1 2020
- Will also enable a second development pathway: the prevention of the immunogenicity of biotherapeutics, such as gene therapy products

PREVAIL Part 2 (Lupus) - Design



- Phase 2a Proof-of-Concept in Lupus
- Lupus is quintessential chronic autoimmune disorder driven by auto-reactive B cells
- Polymorphisms in CD32B heavily associated with lupus

Anti-IL15 for diet non-responding celiac disease

Fully-human anti-IL-15 monoclonal antibody

- 21-day half-life, with sub-cutaneous administration every 2-4 weeks

Proof of Concept (POC) Established

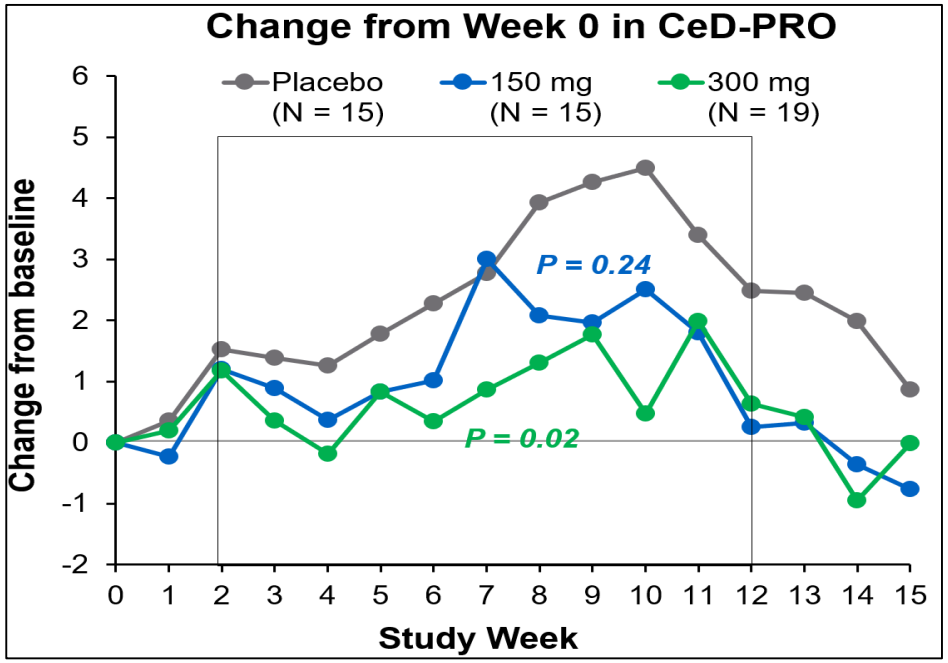
- Well tolerated in six prior clinical trials with ~300 patients
- Achieved POC in Phase 2a studies in non-responsive celiac disease and no known dose-limiting toxicity
- Also POC in refractory celiac disease Type II (in situ T cell lymphoma)

Status

- Expect to initiate Phase 2b trial in Q2 2020
- Amgen has the right to re-acquire PRV-015 for $150 million up-front, milestones and royalties

Safety and efficacy of AMG 714 in adults with coeliac disease exposed to gluten challenge: a phase 2a, randomised, double-blind, placebo-controlled study.
Lahdeaho et. al. Lancet Sep 2019 DOI:https://doi.org/10.1016/S2468-1253(19)30264-X.

Phase 2a data shown at 2018 DDW, published in *Lancet*



Gluten Challenge Study:
Week 0-2 Gluten-Free cookies; Week 2-10 Gluten-Containing cookies

Highly statistically significant across multiple celiac and gastrointestinal endpoints, as well as local inflammation

Phase 2b PROACTIVE study design

Objective

- Dose-Finding Phase 2b study testing 3 dose levels of PRV-015 against placebo (1:1:1:1)

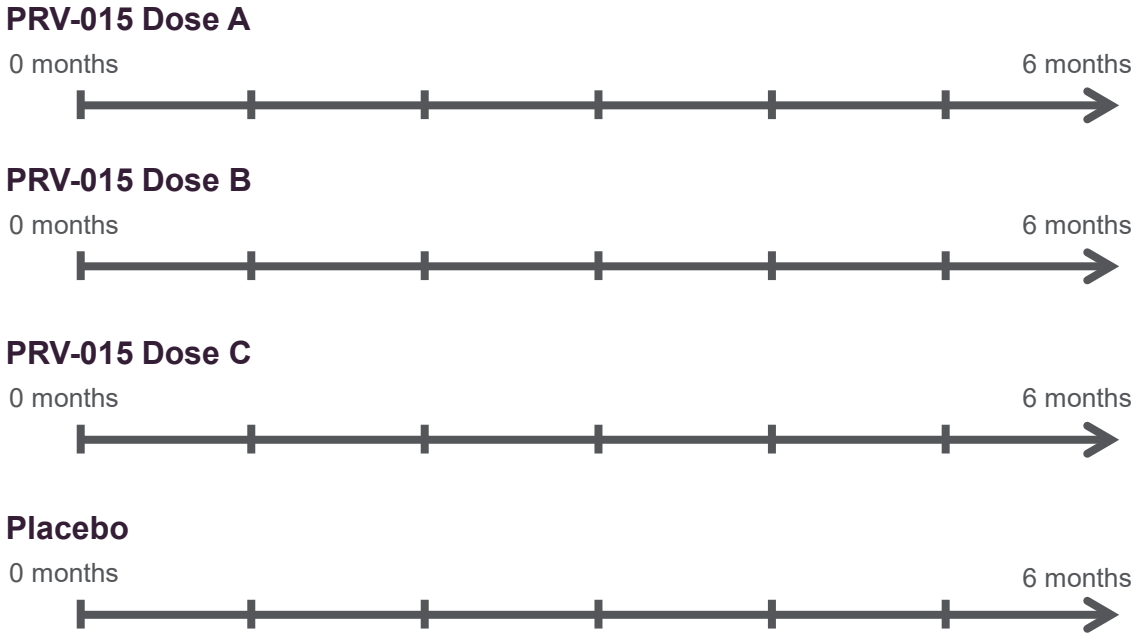
Primary Endpoints

- Validated CeD-PRO (Celiac Disease Patient Reported Outcome) (GI symptoms)

Secondary Endpoints

- Symptoms: BSFS Score
- Inflammation (IELs: intraepithelial lymphocytes)
- Histology
- Safety

Trial Design



- ~220 subjects in a dose-finding 4-arm study (3 PRV-015 arms, 1 placebo arm)
- Adult celiac patients not responding to the Gluten Free Diet
- 6 months treatment duration via subcutaneous injection every other week
- Planned to commence in Q2 2020

Financials

Financing history

- Follow-on Financing (Sep ’19) generated $62.7 mil of net proceeds
  - $20.0 million from Amgen
  - $42.7 million from equity capital markets
- IPO (Jul ’18) generated $59.3 mil of net proceeds
- Series A (Apr ’17) provided $26.7 mil of net proceeds

Ownership and capital structure

- 47.6 million shares outstanding
- 55.6 million shares fully diluted
- All directors and officers as a group own ~11%

Virtual company with 19 full-time employees as of February 2019

Balance sheet

- $95.1 million of cash as of September 30, 2019
- No debt

Operations

- Projecting $10–$12 million of cash used in operations for Q4 2019
- Net cash operating expenses of $31.9 million in first nine months of 2019
- Net loss of $32.7 for the nine months ended September 30, 2019

Team of experienced scientists and developers

Ashleigh Palmer
CEO and Co-founder

30+ yrs in Biopharma,

Previously, CEO of INO Therapeutics, bought by Ikaria, finally by Mallinckrodt for $2.3B

At INO took inhaled NO for neonatal hypoxia through Phase 3 development, approval and launch, reaching $250M in first 2 years

Executive Chairman and co-founder of Celimmune, focused on celiac disease and later sold to Amgen

Francisco Leon
CSO and Co-founder

Basic and clinical immunologist by training

Drug developer at BMS, pre-AZ MedImmune, and Centocor/Janssen, with 20+ yrs experience, and 5 drugs on the market.

Co-founded Celimmune, focused on Celiac disease, as CEO and CMO and ran two Phase 2 trials for our anti-IL-15, later acquired by Amgen

Eleanor (Leni) Ramos
CMO

Transplant nephrologist

Drug developer at BMS and Roche, with 25+ yrs including 5 drugs currently on the market

CMO at both ZymoGenetics, acquired by BMS for $1B, and Global Blood Therapeutics

Previously ran all clinical trials for immune tolerance induction at ITN with Jeff Bluestone, including teplizumab

Andrew Drechsler
CFO

20+ yrs in Biotech

Previously, CFO of Insmed-2012-2017, took company from $100M to $1B company, raised $400M in public markets, and built org from 30 to 175 employees

Father of three T1Ds and personally involved with JDRF

Jason Hoitt
CCO

18 yrs in Biotech

Previously, CCO of Dova which was acquired Sobi in Q4 2019

Commercial leadership roles at Insmed, Sarepta, Vertex, and Gilead.

Launches include DOPTELET, Arikayce, Exondys 51, and Incivek

Corporate

2020 milestones

2020

PRV-3279
Top-line results of Phase 1b safety cohort

PRV-015
Initiate Phase 2b trial in non-responsive celiac disease patients

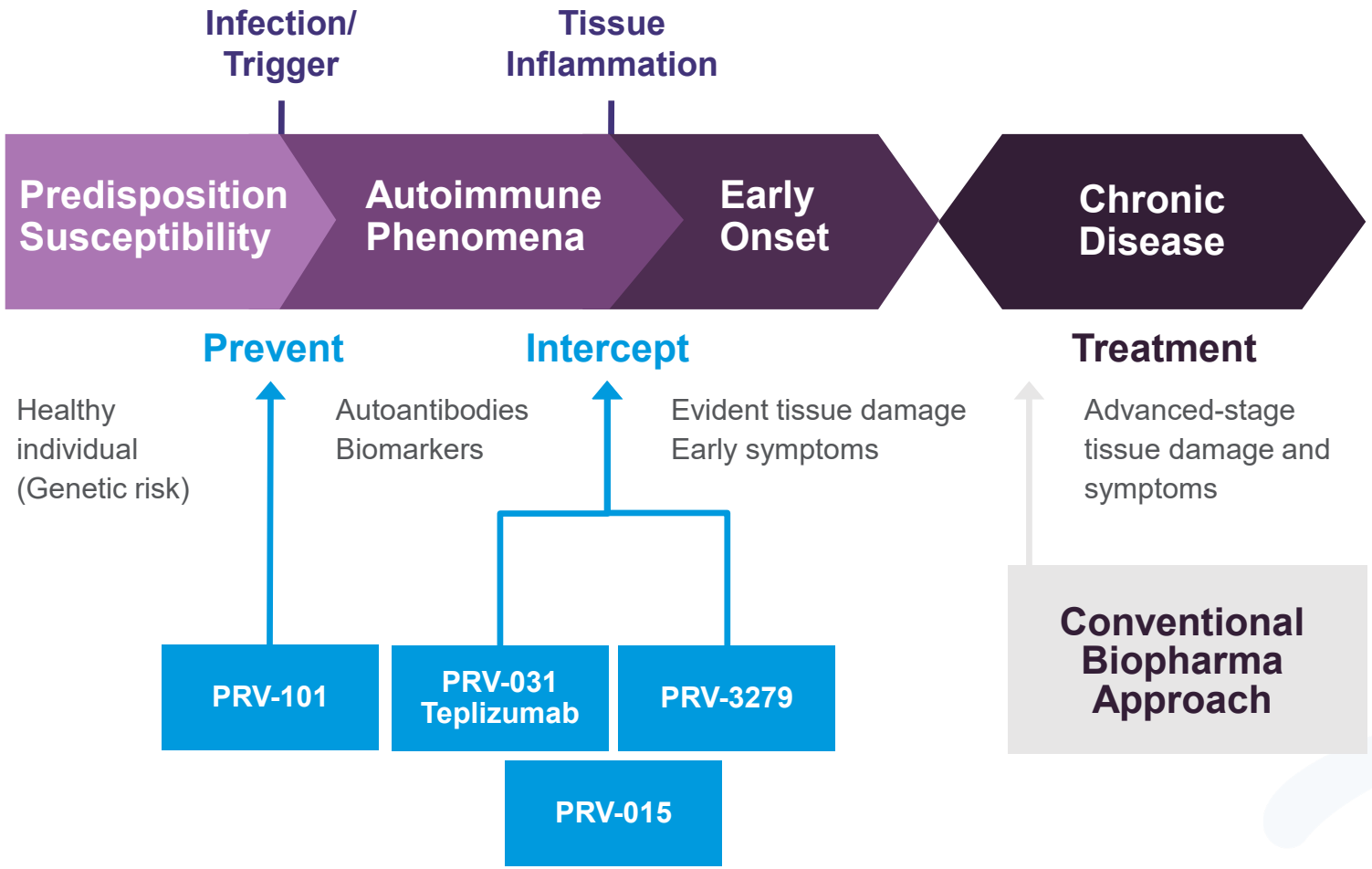
PRV-101
File IND and initiate Phase 1 trial for coxsackie virus vaccine in healthy subjects

PRV-031
Submit BLA* for teplizumab in at-risk Type 1 diabetes patients

*** teplizumab US approval expected in 2021 based on potential priority review**

Summary

Provention's Interception/Prevention Paradigm



Significant investment upside across all 4 programs

- PRV-031 (teplizumab)
  - For the delay or prevention of T1D
    - Projecting BLA filing Q4 2020; potential approval in mid-2021. Opportunity >$1B in the US alone for at-risk T1D indication
  - Multiple expansion opportunities, including in newly-diagnosed T1D
- PRV-3279 a bispecific targeting B-cell driven disease with multi-indication potential
- PRV-101 a vaccine for the prevention of coxsackie virus and potentially T1D/celiac
- PRV-015 a mAb for non-responsive celiac disease

Strong financial position

- $95.1 million of cash at 9/30/2019

Thank you

proventionbio