About the CNP-103 Clinical Trial

For Healthcare Professionals

Study Purpose

The purpose of the CNP-103-CL-201 (CNP-103) Clinical Trial is to evaluate the **safety, tolerability, pharmacodynamics, and efficacy** of an investigational study therapy, CNP-103, in participants ages 12–35 with recent onset Stage 3 type 1 diabetes (T1D).

Study Design

This is a phase 1b/2a, randomized, double-blind, placebo-controlled study that is enrolling approximately 72 participants across 2 phases. The phase 1b dose-escalation portion will recruit 36 participants randomized at a 2:1 ratio (active:placebo), followed by a phase 2a expansion phase of 36 participants with a 3:1 ratio. The total duration of participation will last approximately 13 months, which includes a screening period (28 days), treatment period (90 days), and follow-up period (275 days). All participants will attend 10 study site visits throughout the study duration.

The investigational study therapy, CNP-103, is administered via IV infusion on Days 1, 8, and 90 during the dose-escalation phase. Expansion phase dosing will be established based on results from the dose-escalation phase.

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Key Eligibility Criteria

Inclusion

- Ages 12–35 years (inclusive)
- Diagnosis of Stage 3 T1D within 180 days prior to study enrollment according to ADA criteria
- On standard of care diabetes management including insulin therapy as a routine, a nutrition plan, regular exercise, or other relevant specialty care
- Peak stimulated C-peptide > 0.2 nmol/L measured from a Mixed Meal Tolerance Test (MMTT)
- Participants on systemic corticosteroids or any medication used to treat symptoms of T1D (other than insulin) must undergo a washout period of at least 2 weeks

Exclusion

- Within 90 days prior to first dose:
  - Oral immunomodulators: cyclosporin, azathioprine, methotrexate
  - Other antidiabetic agents besides insulin within 90 days prior to screening
- Within 12 months prior to first dose:
  - T cell–modifying immunotherapy (e.g., abatacept, etanercept, ustekinumab)
  - T cell–depleting immunotherapy (e.g., teplizumab)
- History of or currently active immune disorders other than T1D (including autoimmune disease), unless deemed acceptable by the medical monitor
- Pregnancy
- Significant comorbid conditions, which, in the investigator's opinion, make the participant unsuitable for study participation

Additional eligibility criteria, according to approved protocol, will apply.

About the Study Therapy

CNP-103 is an investigational therapy being evaluated to determine whether antigen-specific immune tolerance can reduce autoimmune-mediated β cell destruction and preserve endogenous insulin production in patients with recent-onset type 1 diabetes (T1D).[1,2]

Exogenous insulin remains the standard of care for T1D but only provides symptomatic glucose control and requires lifelong administration without addressing the underlying autoimmune process.[3]

CNP-103 is designed to induce immune tolerance to the 4 major β cell autoantigens in T1D by addressing the heterogeneity of autoimmune responses observed in T1D including:

- Preproinsulin (PPI)
- Glutamic acid decarboxylase 65 (GAD65)
- Islet-specific glucose-6-phosphatase catalytic subunit–related protein (IGRP)
- Zinc transporter 8 (ZnT8)

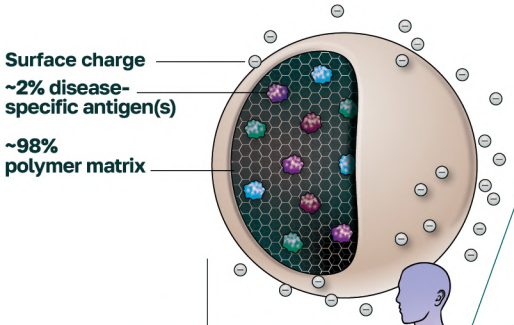
Sustained β cell function has been shown to be associated with improved glycemic control and a reduced risk of hypoglycemia, diabetes ketoacidosis, and long-term complications.[4] By halting the autoimmune-mediated destruction of pancreatic β cells, CNP-103 has the potential to preserve β cell function and consequently endogenous insulin secretion.[1,2,3]

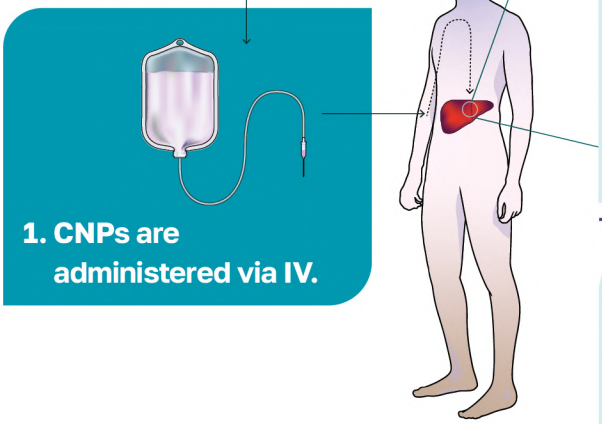
How CNP-103 Works

Mechanism of Action Harnesses Normal Bioclearance and Tolerance Pathway[2,3]

COUR nanoparticles (CNPs)

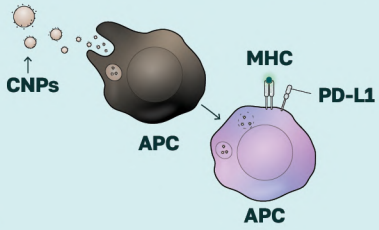
CNPs mimic apoptotic bodies based on size (~500 nm) and negative charge leading to tolerogenic signal.





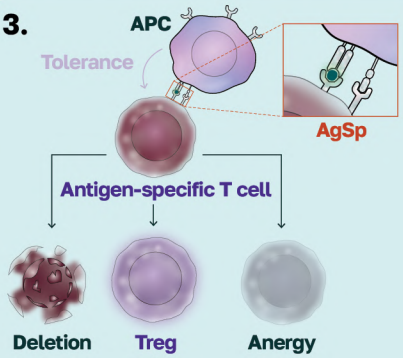
1. CNPs are administered via IV.

2. In the Liver and Spleen



Negatively charged CNPs are phagocytosed by antigen-presenting cells (APCs), where they are degraded, and the peptide fragments are then presented to T cells on the surface via Major Histocompatibility Complex (MHC).

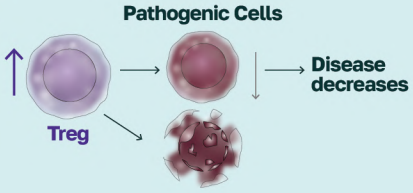
3.



APCs present the antigens in the context of the tolerogenic signal, resulting in antigen-specific reprogramming of pathogenic T cells. T cells then undergo deletion, anergy, or activate a T-regulatory (Treg) response through this endogenous mechanism for maintaining peripheral tolerance.

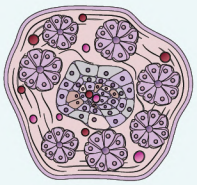
Tregs traffic to site of disease

4. Site of Disease



Down regulation of autoimmune activity at disease sites: These effects are intended to reduce immune-mediated/ T cell–mediated β cell destruction in pancreatic islets.[4]

TYPE 1 DIABETES
PANCREATIC ISLET CELLS



The CNP-103 Clinical Trial evaluates whether targeted, antigen-specific immune tolerance can:

- Modify the underlying autoimmune process in Stage 3 T1D (pharmacodynamics)
- Preserve remaining endogenous insulin secretion (efficacy)

Refer a Patient

If you have a patient who may be eligible for this study, please refer them to **T1D103clinicalstudy.com** to complete the prescreener and find out if they prequalify. You can also visit **ClinicalTrials.gov** (NCT06783309) or **T1D103clinicalstudy.com** to contact a research site for more information.

Each potential participant will be required to have a screening visit with the study doctor to see if they qualify. Those who do qualify and enroll will receive the assigned study treatment and study-related care at no cost to them or their families. Any patients you refer to this study will be seen for study-related reasons only.

1. Roep BO, Wheeler DC, Peakman M. Antigen-based immune modulation therapy for type 1 diabetes: the era of precision medicine. *Lancet Diabetes Endocrinol*. 2019;7(1):65-74. doi:10.1016/S2213-8587(18)30109-8.
2. Podojil JR, Genardi S, Chiang MY, et al. Tolerogenic immune-modifying nanoparticles encapsulating multiple recombinant pancreatic β cell proteins prevent onset and progression of type 1 diabetes in nonobese diabetic mice. *J Immunol*. 2022;209(3):465-475. doi:10.4049/jimmunol.2200208.
3. Jamison BL, Neef T, Goodspeed A, et al. Nanoparticles containing an insulin-ChgA hybrid peptide protect from transfer of autoimmune diabetes by shifting the balance between effector T cells and regulatory T cells. *J Immunol*. 2019;203(1):48-57. doi: 10.4049/jimmunol.1900127.
4. Lachin J. *Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC)*. Version 21, NIDDK Central Repository; 2021. doi:10.58020/mn8k-ms49.

COUR PHARMA