RFA: Accelerating clinical trials evaluating disease-modifying therapies for T1D

Informational Webinar

August 28, 2024

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Agenda

1. RFA Background and Strategy
2. Funding Mechanism
3. Project Eligibility
4. Administrative Wrap-up
5. Q&A

Background & Strategy

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As we drive toward curing type 1 diabetes, we help make everyday life better for the people who face it

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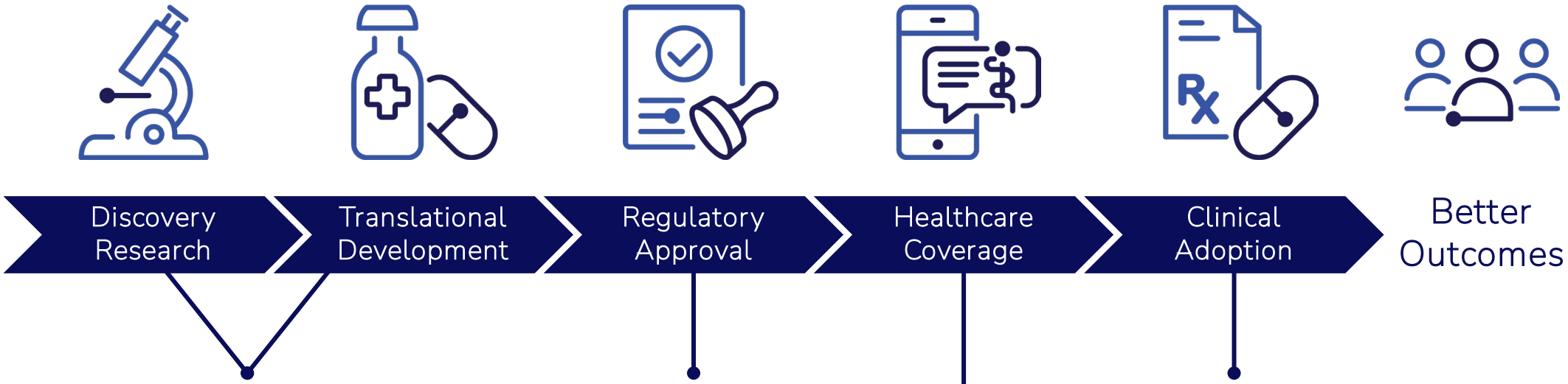
Driving Research Along the Pipeline



- Fund research
- Advocate for government funding for research
- Invest alongside for-profit funders in T1D products
- Advance clinical trials

- Improve prospects for regulatory approval

- Increase coverage, affordability, and choice

- Supporting continuing healthcare provider education
- Educate community

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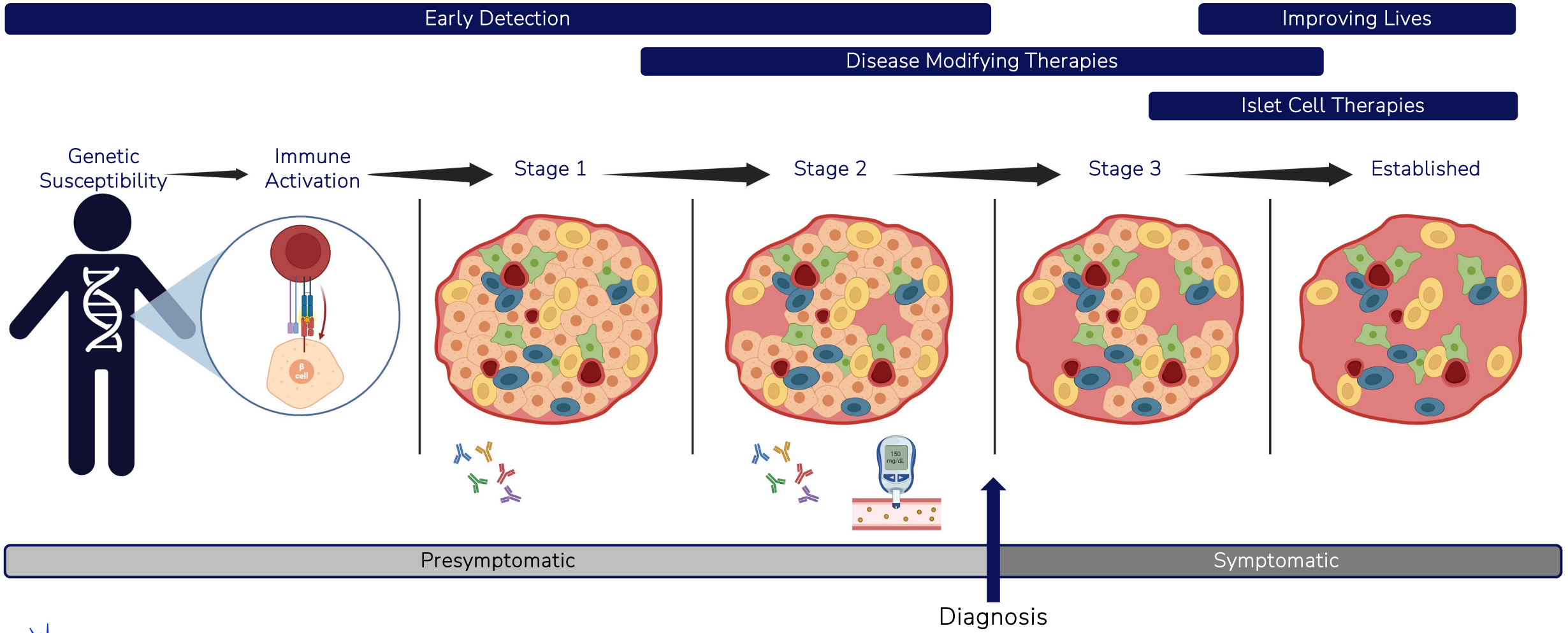
Research Project Area by Disease Stage



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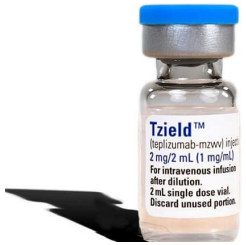
Advances in Disease-Modifying Therapies

There have been a number of recent advances in the clinical assessment of disease-modifying therapies for T1D



Teplizumab (Tzield) approved for individuals prior to clinical diagnosis (Stage 2) T1D (only DMT approved)

In addition, 7 disease-modifying therapies have shown efficacy following diagnosis (stage 3) in clinical trials

- Teplizumab
- Abatacept
- Verapamil
- Rituximab
- Anti-thymocyte globulin (ATG)
- Baricitinib
- Golimumab

This highlights that interventions aimed at rebalancing the immune system to disrupt autoreactivity and/or to support endogenous beta cells have the potential to modify the course of disease and provide for the extension of beta cell function to delay or halt T1D progression.

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There is a remaining unmet need in the development of disease-modifying therapies for T1D

A significant deficit in the transition of therapies from Phase 2 to Phase 3 trials and registrational approval

There has been limited success in moving strategies to induce tolerance from preclinical studies into the clinical setting.

Approaches focused on enhancing the regulatory elements of the immune system have shown mixed efficacy in human trials.

Approaches to regenerate beta cells to increase functional beta cell mass have shown preclinical promise, however clinical translation has been delayed due to the need for targeted delivery to overcome safety concerns.

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Breakthrough T1D: Driving progress

Clinical development of disease-modifying therapies through strategic funding initiatives

- Building a robust clinical pipeline and accelerate the transition of therapies from preclinical to clinical development.
- Establishing efficacy and safety for approved therapies that have shown efficacy in other autoimmune diseases for T1D.
- Promoting the development of combination therapies.
- Providing critical additional data for the validation of C-peptide as a validated surrogate endpoint to demonstrate clinical benefit in T1D.
- Establishing efficacy and identify markers of response to develop a path for testing therapies earlier in disease, or in combination with cell replacement therapy and to support higher efficiency in trials.

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Funding Opportunity

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Purpose:

Breakthrough T1D is seeking Letters of Intent (LOIs) from academic and/or industry applicants for clinical trials to evaluate drugs and biologics to delay, halt, or reverse T1D through supporting or expanding endogenous beta cell survival and function, disrupting autoimmune pathology, or combinations of the above.

Mechanisms:

1) Strategic Research Agreement (SRA)
   - Up to 10% for indirect costs
2) Industry Discovery and Development Partnership (IDDP)
   - No indirect costs allowed

Grant Handbook

https://www.breakthrought1d.org/granthandbook/

Breakthrough T1D Research Strategy

https://www.breakthrought1d.org/explore-research/research-strategy/

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Trials Supported:

A. Proof of Concept (POC) to enable further clinical development.

B. Phase 1 Trials to determine safety.

C. Phase 2 Trials to determine efficacy.

Budget and Scope:

Applicants may request budgets of up to $1.5M per year, for up to 4 years.

Budget and timeline must be commensurate with and justified for the trial design, phase of development, and target enrollment.

Funding will be provided according to milestone-based payments.

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Clinical Study Guidelines

All submissions must follow the US National Institutes of Health (NIH) guidelines for studies including human subjects, including the common rule changes (Breakthrough T1D Grant Handbook)

In addition, the following will be required for project consideration:

- Include an experienced clinical trial manager (CTM) in the trial budget.
- Depending upon the study phase, be powered for the assessment of stimulated C-peptide AUC at endpoint.
- Include an extension period for follow-up measures to for evaluation of durability of response where appropriate.
- Include the use of continuous glucose monitors (CGMs) for all participants.
- Include the assessment of HbA1c, Time in Range, Insulin Dose, and other measures of metabolic function as appropriate.
- Adhere to a harmonized sample collection plan for potential future analysis (will be provided to those invited to full proposal).

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Project Eligibility

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Applicant Eligibility

Applications may be submitted by:
- Domestic and foreign non-profit organizations, public and private, such as universities, colleges, hospitals, and laboratories.
- For-profit industry entities.
- Units of state and local governments, and eligible agencies of the federal government.

Applicants:
Must hold an M.D., D.M.D., Ph.D., or equivalent and have a faculty position or equivalent at a college, university, medical school, or other research facility.
* There are no citizenship requirements for this program*

Collaborations:
Breakthrough T1D encourages collaborative approaches, including between academic applicants and industry partners, and multi-country collaborations.

To assure continued excellence and diversity among applicants and awardees, we strongly encourage applications from persons with disabilities, women, and members of minority groups underrepresented in the sciences.

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Proposals sought under this RFA

Examples of proposals appropriate for this RFA include (but are not limited to):

- Trials evaluating novel small molecule drugs or biologics in people with T1D.
- Trials repurposing small molecule drugs or biologics with demonstrated efficacy in non-T1D populations that have clear rationale or preclinical data for assessment in T1D.
- Inclusion of people with T1D in existing trials evaluating small molecule drugs or biologics in a non-T1D population.
- The inclusion of an additional arm to an ongoing T1D trial to test an additional intervention or new patient population.
- T1D-focused real work studies collection efficacy and safety data on drugs or biologics with expected benefits for people with T1D.

Priority consideration will be given to trials that evaluate:

- An immune agent or therapy with established efficacy in another autoimmune disorder for a novel assessment to disrupt the immune attack on islets and preserve beta cell function in individuals newly diagnosed with T1D.
- Multiple agents that have individually shown efficacy in reducing/halting autoimmunity or supporting beta cell health in a combinatorial approach with a clear rationale for increasing efficacy through synergistic or additive mechanisms.
- Proven beta cell regeneration agents with novel targeting strategies based upon strong preclinical data with a focus on establishing a safety profile for the targeted regenerative therapy.
- Trials that include the assessment of exploratory endpoints.

Proposals that will not be considered

Examples of research that will not be considered for the RFA include:

- Trials not aligned with the Breakthrough T1D Research Strategy.
- Non-clinical, preclinical, or observational studies.
- Clinical trials that do not include people with T1D (however, trials may include other populations in addition to people with T1D).
- Trials assessing therapies in populations other than Stage 3*.
- Trials assessing combinations of more that 2 interventions*.
- Trials assessing nutraceuticals such as Vitamin D as a monotherapy.
- Trials evaluation lifestyle interventions such as diet and exercise.

* Unless approved by Breakthrough T1D staff prior to submission

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Critical Considerations

It is expected that proposed trials will primarily focus on new onset (stage 3) individuals. Clear plan for recruitment must be provided.

Demonstrating that participant numbers and target enrollment should be appropriate for the stage of clinical assessment.

Investigators selected to submit full proposals will be asked to meet with Breakthrough T1D staff to discuss the inclusion of Patient Reported Outcomes (PROs) and to utilize our Participant Advisory Committee (PAC).

Funding will be contingent upon a written commitment from the drug manufacturer to provide study drug and placebo, to be provided with the full proposal.

Choice of surrogate and mechanistic endpoints in the trial should be well justified. Endpoints should align with regulatory pathways either established or under consideration, rather than exploratory objectives.

We encourage proposals that seek to leverage existing or planned clinical trials by adding people with T1D or ancillary studies.

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Review Criteria

Standard Review Criteria:

- Significance
- Approach
- Innovation
- Investigator Experience
- Environment

In addition, LOI's must address, and will be reviewed based upon:

- Justification for choice of trial endpoint(s).
- Targeted participant population, **recruitment strategy**, and inclusion/exclusion criteria.
- Plan for acquiring the drugs and placebo/controls used in the study.

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Tips for Successful LOIs

Familiarize yourself with the most recent T1D literature and Breakthrough T1D Research Strategy.

Don’t waste space in your LOI describing T1D or the need for additional therapies, focus on your approach/rationale.

Familiarize yourself with the SRA/IDDP template and completely answer each section requested.

Begin your application early and ensure that all information is available by the submission deadline.

Develop your proposal based upon the specific requests outlined for this RFA, out-of-scope proposals will not be considered.

Don’t hesitate to contact Breakthrough T1D staff with any questions during the submission process.

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Administrative Wrap-up

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Submission Instructions

Applicants should register and submit their completed LOI in RMS360

- If you have issues logging in, please contact Karen Ng (kng@BreakthroughT1D.org)
- All templates and submission instructions/materials are available in the portal.
- No extensions for submission of LOIs or Full Proposals will be given, so please register and begin the submission process well in advance of the deadline.
- An approved LOI is required prior to submission of a full proposal.

https://breakthrought1d.smartsimple.us/

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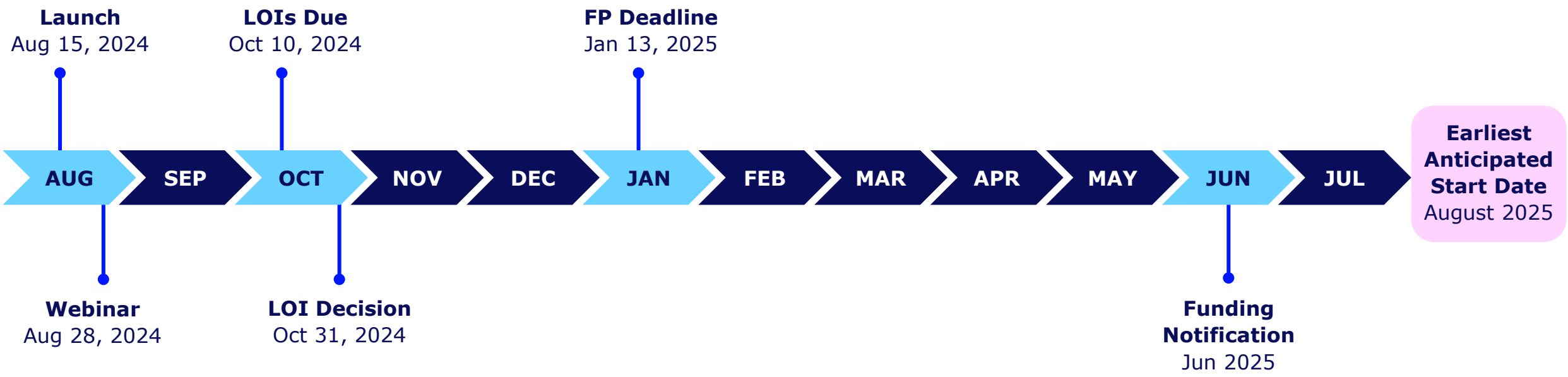
Award Timeline



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Thank you

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