Goldfinch Bio
Saving Kidneys, Ending Dialysis

Phase 1, Randomized, Controlled Trial of GFB-024 in Healthy Overweight and Obese Participants and in Participants with Type 2 Diabetes Mellitus

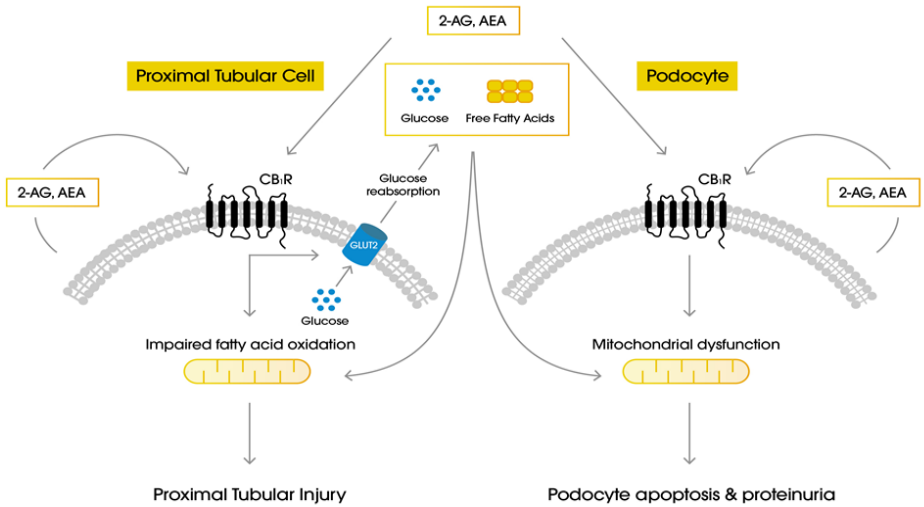
Gregory A. Gaich[1], John Lawler[1], Yossi Dagon[1], Thomas A. Gustafson[1], Leslie Johnson[1], Lori Rudolph-Owen[1]

[1]Goldfinch Bio Inc, Cambridge, MA, United States.

KIDNEY WEEK 2021

Role of Endocannabinoids and Kidney Disease

Elevated circulating endocannabinoids and autocrine CB1 activation results in podocyte and tubular cellular injury

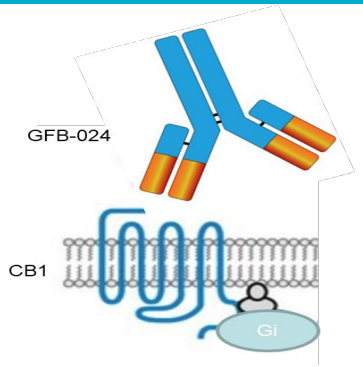


Past CB1 antagonists:

- Showed improved metabolic parameters and reduced weight in patient with obesity
- Prevented proteinuria increases, reduced glomerular injury and kidney hypertrophy in animal models
- Limited by significant CNS-related side effects

FFA=Free Fatty Acids; 2-AG=2-Arachidonoylglycerol; AEA=N-Arachidonoylethanolamine (anandamide).
Adapted from Hwang et al. 2015 and Galadari, et al. 2016

RATIONALE FOR GFB-024 IN PATIENTS WITH DIABETIC NEPHROPATHY

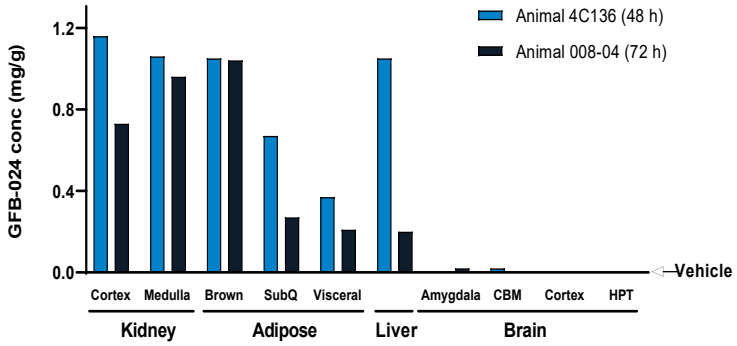


GFB-024 is a recombinant humanized monoclonal immunoglobulin gamma (IgG)1 antibody with specificity for the cannabinoid-1 receptor (CB1).

Peripheral restricted, thereby potentially reducing the risk for CNS associated adverse effects that could occur with a centrally active moiety.

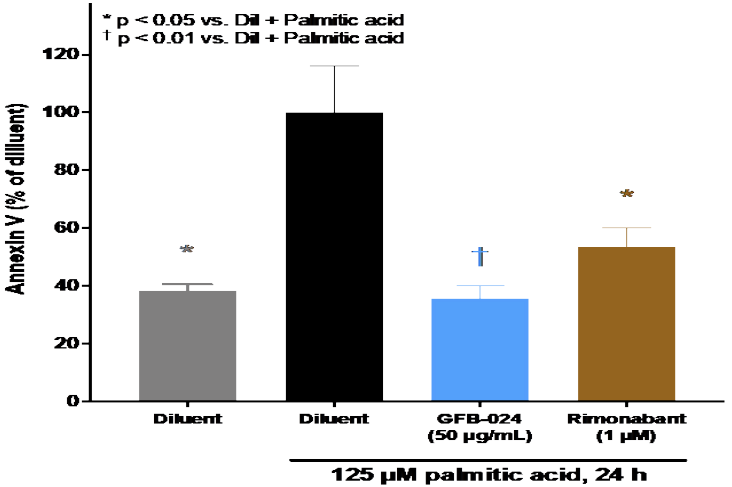
Preclinically, inhibition by CB1 inverse agonist ameliorates diabetes-induced albuminuria, inhibits renal fibrosis and inflammation, and prevents podocyte damage and dysfunction.

GFB-024 is found in peripheral tissues with minimal brain exposure



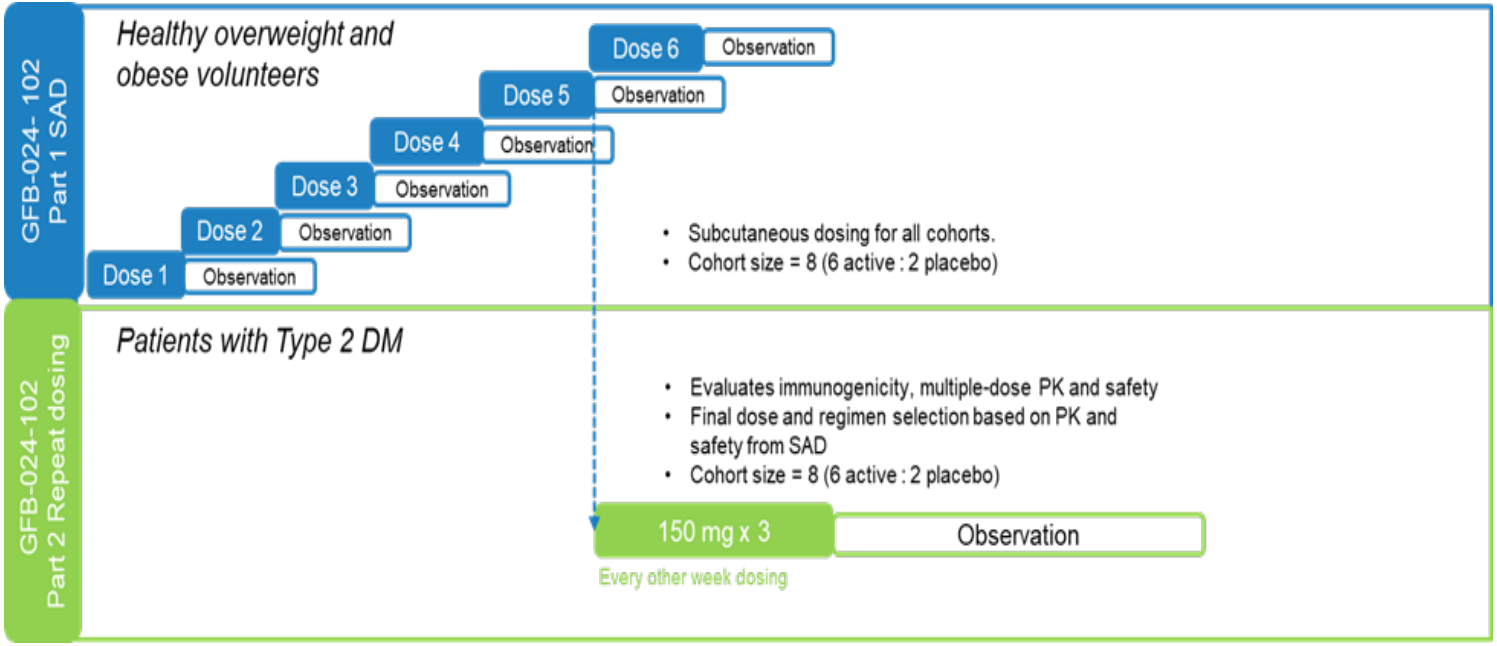
SubQ = subcutaneous
CBM = cerebellum
HPT = hypothalamus

GFB-024 attenuates podocyte cell death induced by palmitic acid, a mediator of diabetic lipotoxicity



GFB-024 First-in-Human Study Design

This is a phase 1, randomized, double-blind, placebo-controlled trial with a single ascending dose (SAD) component to evaluate the safety, tolerability, pharmacokinetics (PK), and immunogenicity of GFB-024 in up to 56 healthy overweight and obese (BMI 25 – 50 kg/m) participants and a repeat-dose component in up to 10 participants with T2DM. (NCT04880291).



GFB-024 First-in-Human Study Design

Study Objectives

- To establish safety, tolerability, and pharmacokinetics (PK) in the single ascending dose (SAD) study in healthy overweight and obese volunteers to support a subsequent repeat-dose exploratory efficacy study in participants with diabetic nephropathy
- To obtain PK, safety, and tolerability data in participants with type 2 diabetes mellitus (T2DM)
- To explore potential phenotypic, genotypic, and biochemical approaches to identifypatients most likely to respond to GFB-024

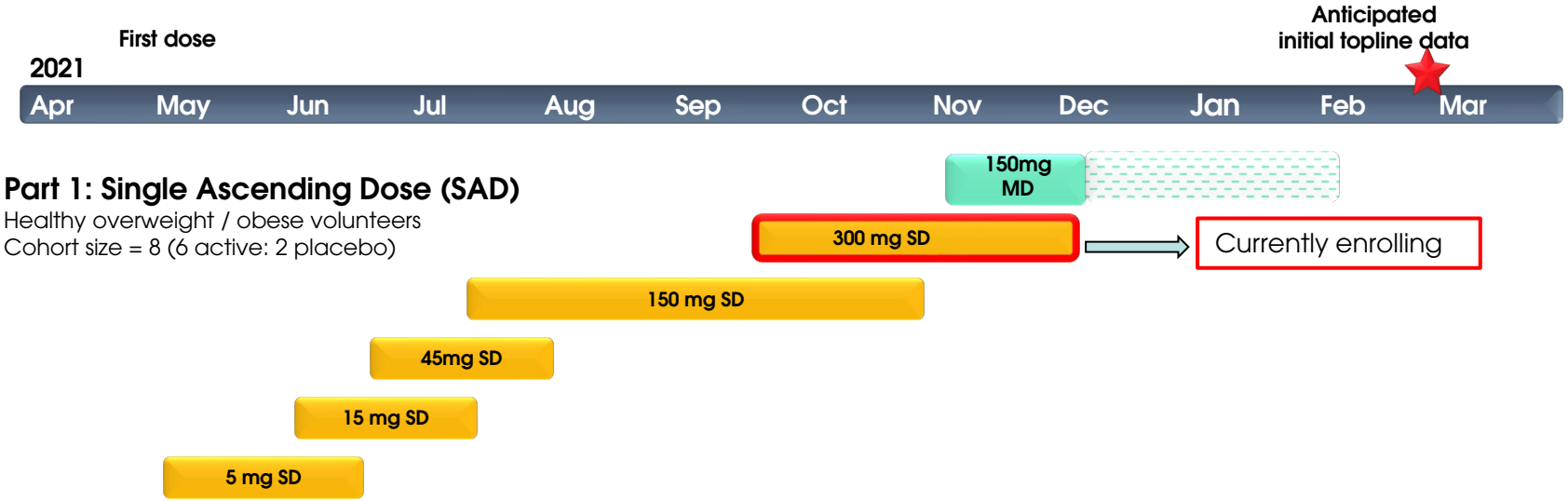
Key Inclusion Criteria

1. 18 to 75 years of age at the time of signing informed consent
2. BMI between 25.0 and 40.0 kg/m^2
3. Estimated eGFR ≥60 mL/min/1.73 m^2
4. SAD cohorts only: in good health, determined by no clinically significant findings
5. Repeat-dose cohort only: T2DM treated with lifestyle modification or metformin and in otherwise good health

Key Exclusion Criteria

1. History of, or treatment for, psychiatric illness, including anxiety or depression within 5 years of the Screening visit.
2. Based on the Columbia-Suicide Severity Rating Scale (C-SSRS), participants with a history of attempted suicide or clinically significant suicidal ideation based on the C-SSRS assessment.
3. SAD cohorts only: Fasting glucose >126 mg/dL.

STUDY ENROLLMENT AND INITIAL FINDINGS



- GFB-024 was safe and well-tolerated in first 4 SD cohorts (up to 150 mg SD)
- GFB-024 PK consistent with monthly SQ dosing
- Blood and fat biopsies being explored for target engagement and patient selection biomarkers
- Results from this trial will provide the foundational evidence to support the clinical development of GFB-024 inpatients with DN driven by CB1 activation.