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**Study Title:** Effect of novel chemical entities on disease progression in a model of Type 1 Diabetes

### Study Objectives

The goal of the study was to test the acute effect of novel compounds on reversing hyperglycemia in a mouse model of compound induced type 1 diabetes.

### INTRODUCTION

Over seventeen million Americans (6.2% of the population) have diabetes. Almost 6 million Americans are unaware they have the disease. There are two main types of diabetes. Both types are caused by problems in insulin levels or function. Type 1 diabetes most often appears in childhood or adolescence and causes high blood sugar when your body can't make enough insulin. Over 90% of all diabetes cases are type 2 diabetes, linked to obesity and physical inactivity. In this form of diabetes, your body makes insulin but cannot use its insulin properly. Over a long period, high blood sugar levels and diabetes can cause heart disease, stroke, blindness, kidney failure, leg and foot amputations, and pregnancy complications. Over 200,000 people die each year of diabetes related complications.

### METHODS AND RECORDS

Following a one week acclimation, mice were injected with novel compound (up to 200mg/kg). Blood glucose was measured 4 days following injection, mice were tested for blood glucose, and mice that exceeded 33mg/day continued onto study, 50 mice were chosen and assigned to groups according to fed blood glucose.

Mice were administered treatments for 4 weeks by oral gavage. Blood was collected by retro-orbital bleed (no more than 50µl) and processed to serum on Days 1, 7, 14, and 28 (at terminus). In the second and fourth week, mice underwent 24 hour urine collection with assessment of microalbuminuria. Following urine collection, mice were tested for Glomerular Filtration Rate (GFR). Mice received an intravenous injection of FITC conjugated insulin with blood draws (no more than 30µl per mouse per time point and not exceeding 1% body weight overall) for analysis of fluorescence at 0, 3, 7, 10, 15, 35, 55, and 75 minutes post-injection.

At the end of the fourth week, mice were euthanized, blood taken, and the left kidney taken and stored in 10% formalin for future analysis.

#### Blood Processing Details:

Blood was processed for serum by collection into non-heparinized hematocrit tubes into serum microtainer tubes, spun for 12 minutes at 12,000 RPMs in a 4°C centrifuge, and then transferred to 0.5 mL microcentrifuge tubes for storage at -80°C until sent for analysis.

#### Treatment Protocol

Gp	n	Treatment	Dose (mg/kg)	Volume (mL/kg)	Dose Route/Regimen
1		Vehicle	n/a	n/a	PO, for 4 weeks
2		Positive Control (Captopril)	50	10	

