

*Inventing, Developing
& Commercializing
Targeted Small
Molecule Drugs in
Cancer, Inflammation &
Metabolic Disease*



Glucokinase Activator ARRY-403

Phase 1 Single Ascending Dose Top-Line Results

August 10, 2009

ARRY-403: Oral Drug for Type 2 Diabetes

Product Profile

- A glucokinase activator (GKA) for Type 2 diabetes
- GKAs control glucose levels via a dual mechanism of action, working through both the pancreas and liver

Target

- Glucokinase senses glucose in the pancreatic beta cells, stimulating insulin release in a glucose-dependent manner
- Glucokinase increases glucose utilization and decreases glucose output in the liver

Preclinical Data

- Demonstrated potent, highly blood glucose level-dependent control of glucose concentrations
- Rapid onset of effect and maximum efficacy within 5 to 8 days
- Additional glucose control achieved when combined with metformin, DPP4 inhibitor or PPAR γ agonist
- No adverse increases of body weight, plasma triglycerides or total cholesterol

Status

- Top-line results available for Phase 1 single ascending dose study in patients with Type 2 diabetes
- Initiating a Phase 1 multiple ascending dose study in patients with Type 2 diabetes

ARRY-403-101

Phase 1 Single Ascending Dose Study

Phase 1 SAD Study in Patients with Type 2 Diabetes

- A Randomized, Single-blind, Placebo-controlled Single Ascending Dose Phase 1 Study to Evaluate the Safety, Pharmacokinetics and Pharmacodynamics of Orally Administered ARRY-403 in Patients with Type 2 Diabetes

Enrollment and Eligibility

- Study start: March 2009
- Population: Patients with Type 2 diabetes
- Genders: Both
- Age: 18 - 65
- HbA1c: <10%

Design

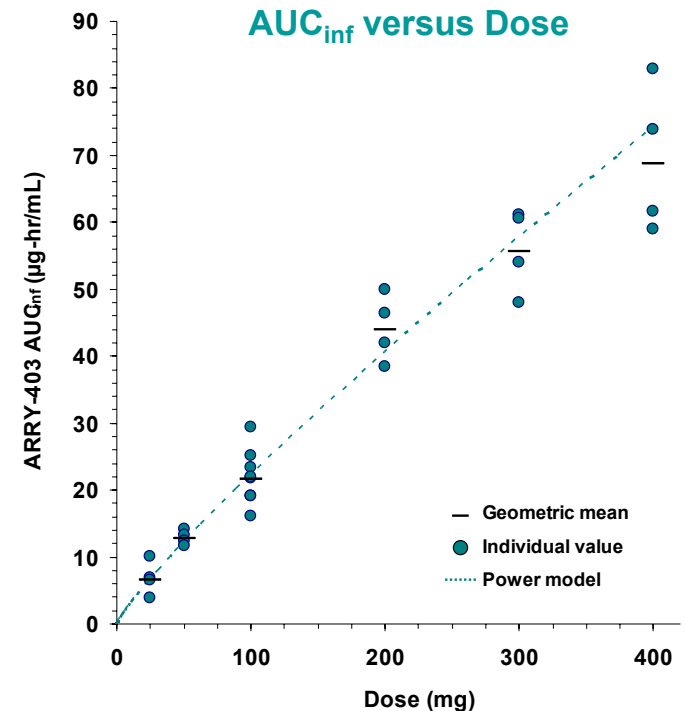
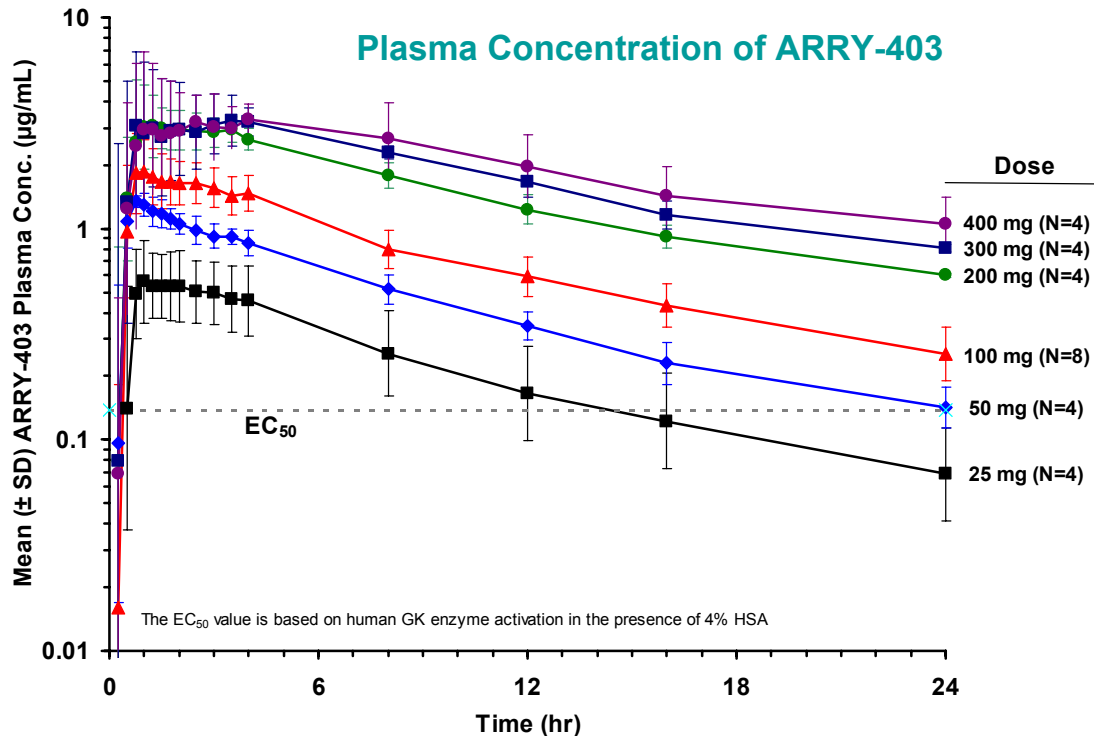
- Dose range: 25 to 400 mg (single dose)
- Dosing: morning mixed meal tolerance test on Day -1 and Day 1, single dose ARRY-403 on Day 1 only
- Randomization: 4 (active) : 2 (placebo) per cohort
- Primary endpoints: safety, pharmacokinetics
- Secondary endpoints: pharmacodynamics (glucose, insulin, C-peptide)

ARRY-403-101 Demographics

Diabetic population characteristics

	Mean \pm SD (N=41)	Range
Age (yrs)	48 \pm 8	27 - 63
Weight (kg)	94 \pm 14	71 - 129
BMI (kg/m ²)	32.3 \pm 2.9	27.1 - 37.7
Fasting blood glucose on Day -1	153 \pm 38 mg/dL	85 – 247 mg/dL
HbA1c (%)	7.5 \pm 1.2	5.3 - 9.9
Gender	25 ♂ : 16 ♀	
Race/Ethnicity	Non-Hispanic White – 11 African American – 8 Hispanic – 21 Asian – 1	

ARRY-403 Exhibits Favorable Pharmacokinetics



Increasing exposure with increasing dose

Low variability in exposure (18% CV)

Coverage sufficient for QD dosing

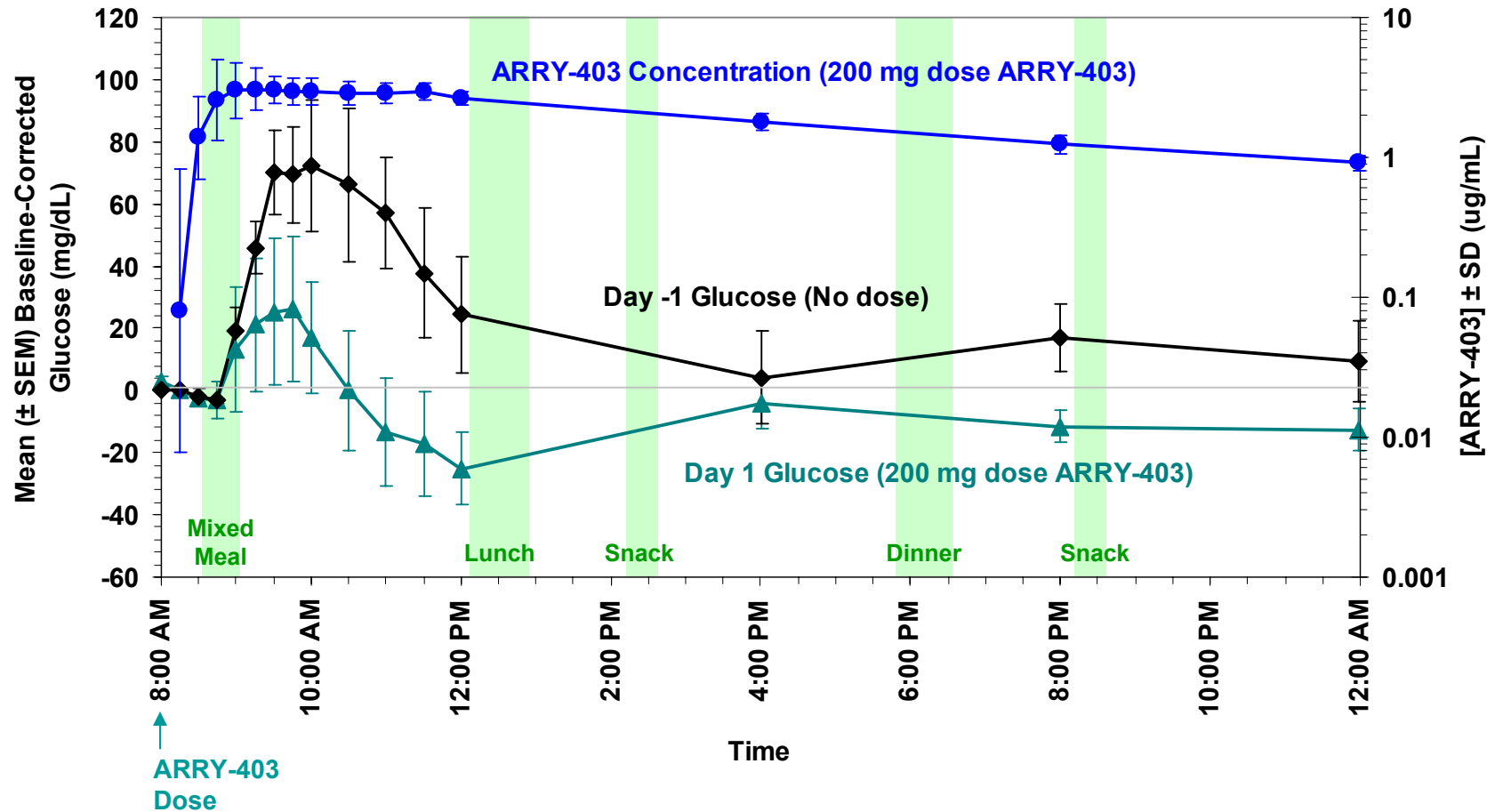
- Plasma concentrations of ARRY-403 $>$ in vitro cell-based EC_{50} for human GK activation for 24 hrs at doses \geq 50 mg

ARRY-403 Achieves Safety Endpoints

Safety Results

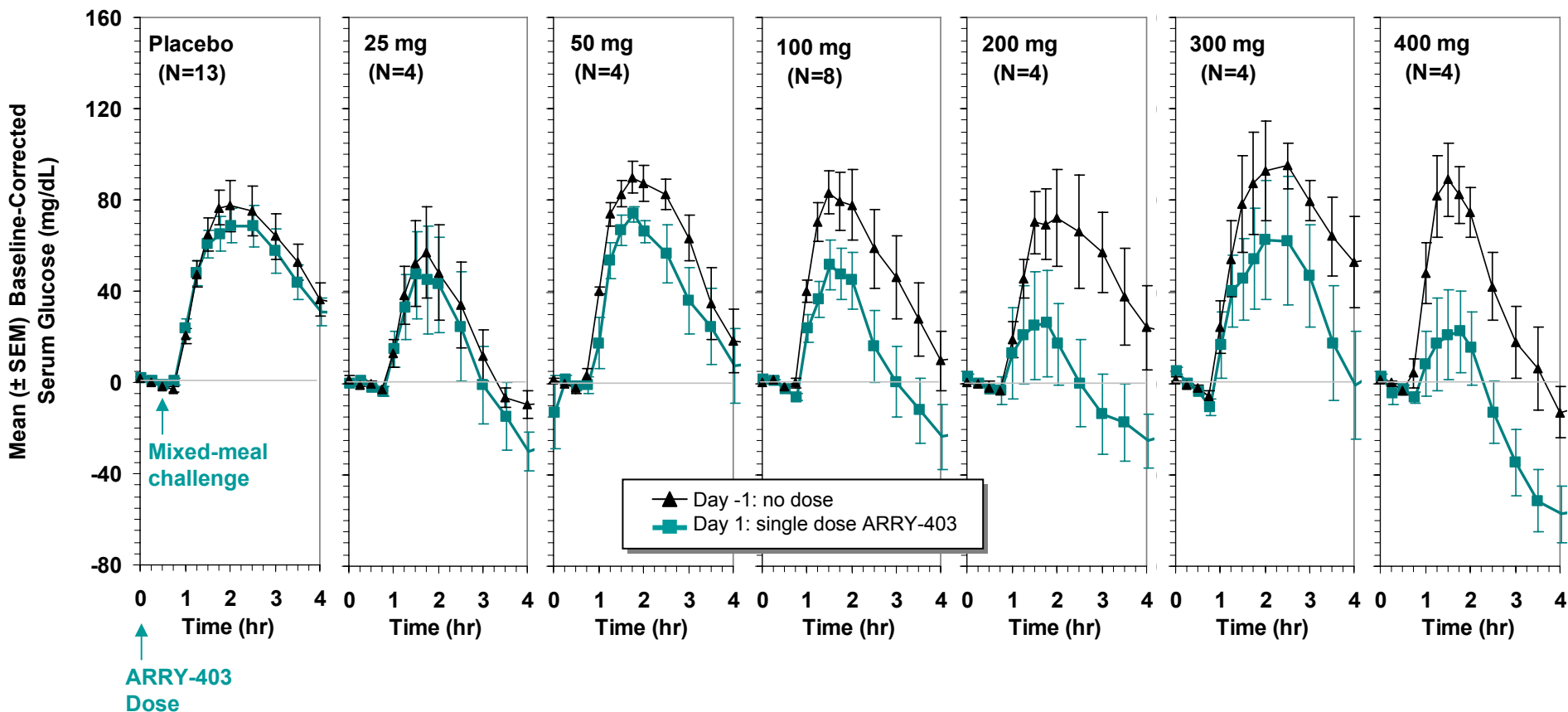
- No patients discontinued the study
- No patterns of abnormal lab values
- No significant changes in ECGs
- No severe adverse events (SAEs)
- One patient at 400 mg dose developed moderate symptomatic hypoglycemia post-dosing that was effectively treated

ARRY-403 Causes Glucose Lowering During Day



Glucose lowered throughout the day

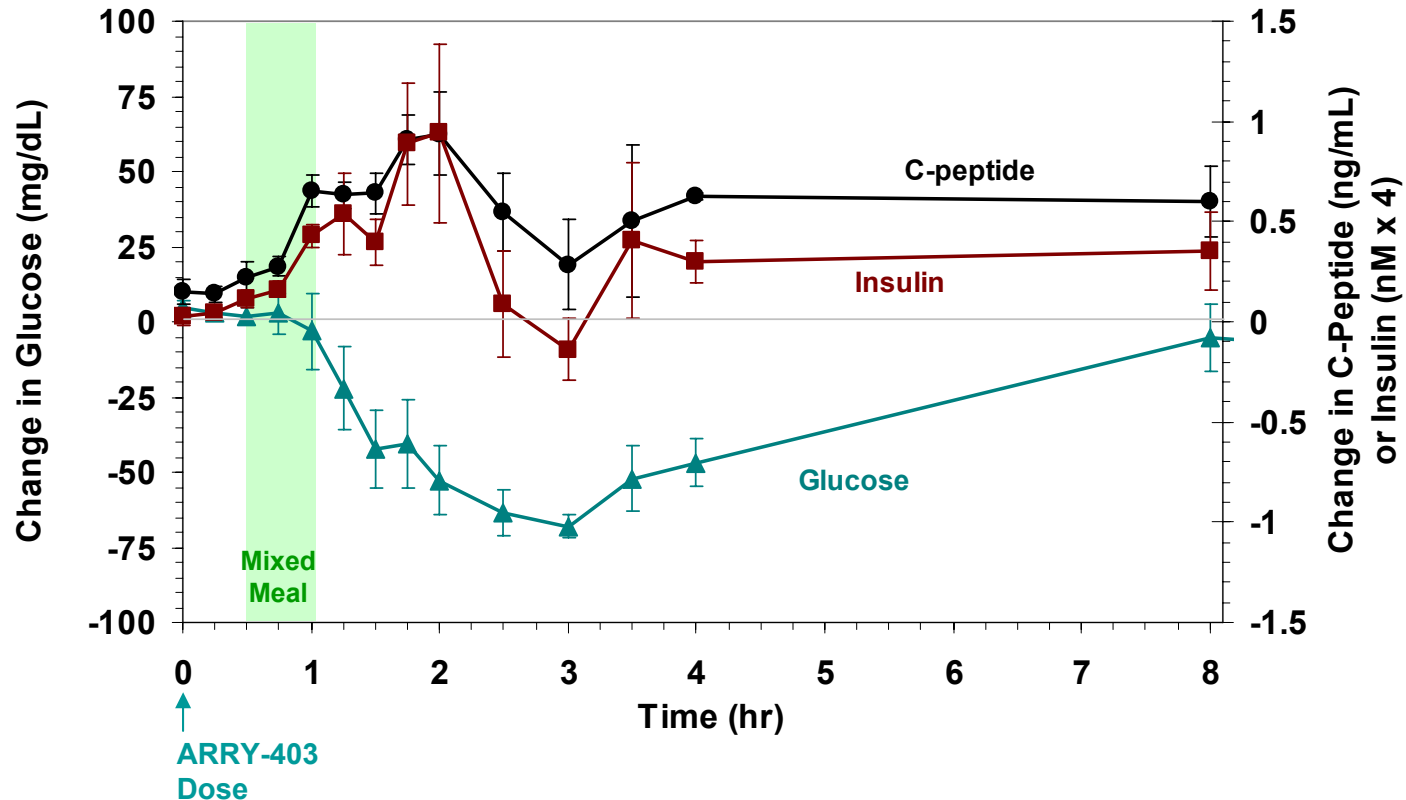
ARRY-403 Decreases Post-meal Glucose Excursion



Significant dose-dependent glucose reduction

ARRY-403 Increases Insulin & C-peptide Levels

Mean \pm SEM Changes Between Day -1 (No Drug) and Day 1 (200 mg ARRY-403):

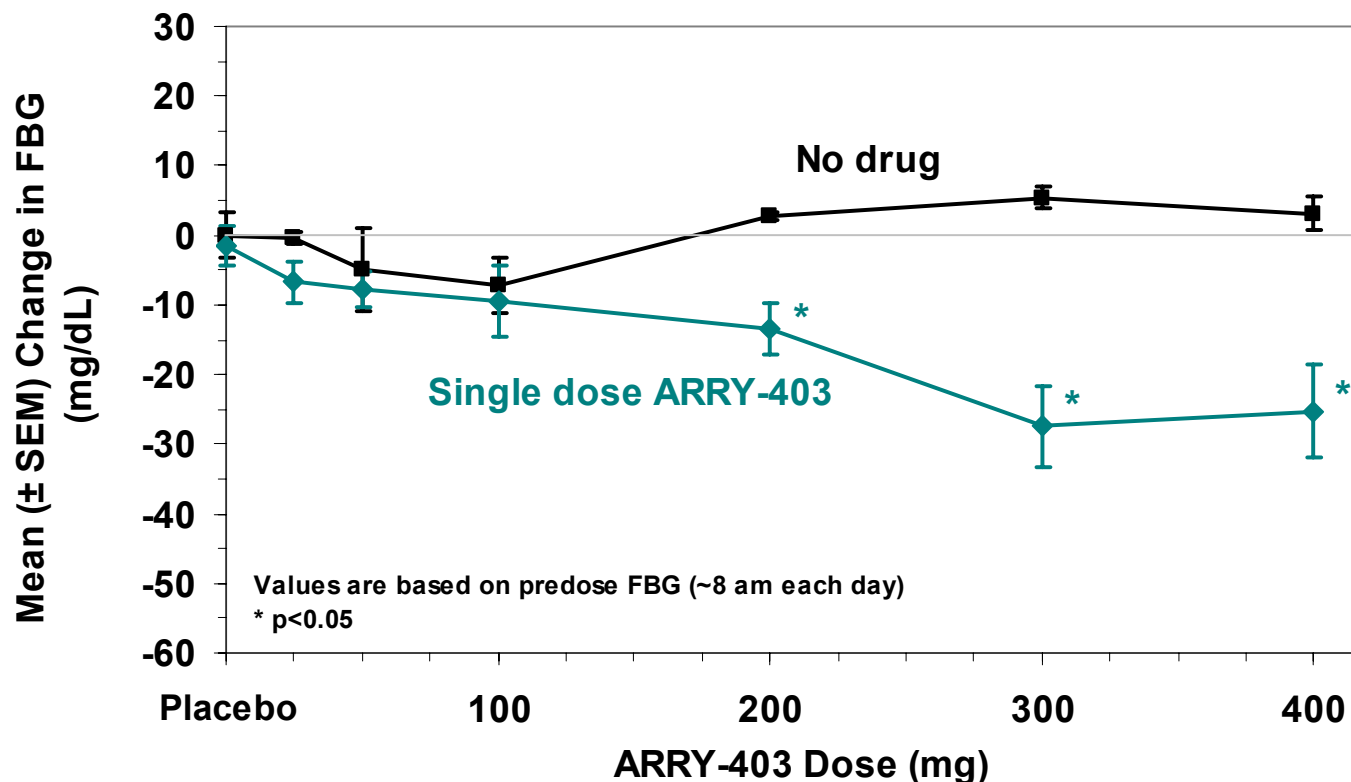


200 mg results are shown as a representative dose level

Increases in insulin and C-peptide consistent with GKA mechanism of action

ARRY-403 Lowers Fasting Blood Glucose

Changes in FBG with and without administration of ARRY-403:



FBG is lowered 24 hrs post-dose at doses of ≥ 200 mg ($p < 0.05$)

ARRY-403 Met All Primary & Secondary Endpoints

Based on this Phase 1 single ascending dose study, ARRY-403 has the following characteristics:

- Increasing exposure with increasing dose
- Low variability in exposure
- Pharmacokinetics consistent with once-daily dosing
- Significant reduction of post-meal and 24-hour fasted blood glucose
- Increases in insulin & C-peptide consistent with the mechanism of action
- Well-tolerated (no serious adverse events)

Initiating a Phase 1 multiple ascending dose study

- Ten day study
- Doses ranging from 10 to 100 mg/day