BCX9250 Phase 1 Trial Results

December 2020

Fibrodysplasia Ossificans Progressiva (FOP)

Devastating Disease; No Treatments Available

Rare disease that **affects approximately 1 in 2 million people** worldwide

Irregular formation of bone or ossification in muscles, tendons or soft tissue

Currently no approved treatments for FOP

Results in loss of function, deformities and **a severely disabling condition**

BCX9250 Phase 1 Healthy Subject Trial Design

- Randomized, double-blind, placebo-controlled, dose-ranging trial in healthy volunteers
- Objective: to evaluate safety, tolerability, and pharmacokinetics of single ascending doses (SAD) and multiple ascending doses (MAD) of orally administered BCX9250

Part 1 – Single ascending dose

- 8 subjects per cohort
  - 6 active, 2 placebo

Dose levels evaluated:

- 5mg
- 10mg
- 15mg (fed and fasted)
- 25mg

Part 2 – Multiple ascending dose, once daily (QD) for 7 days

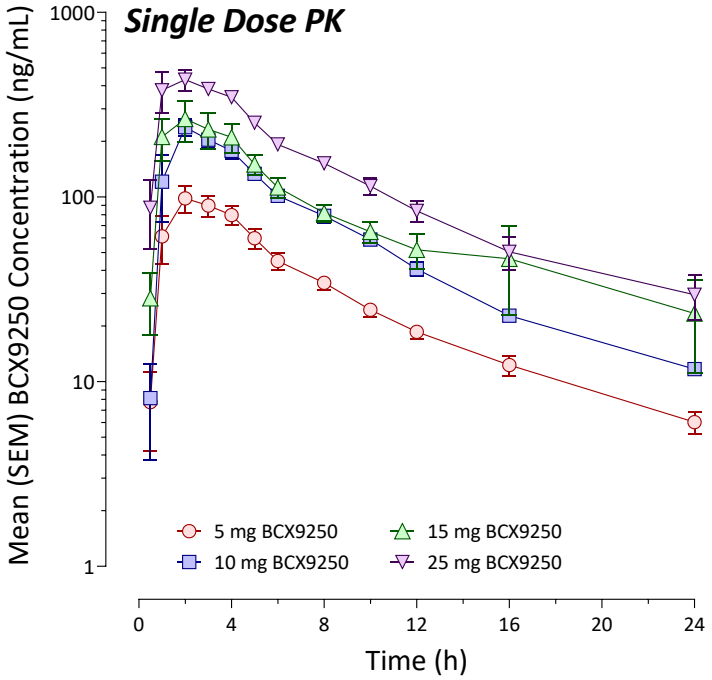
- 12 subjects per cohort
  - 10 active, 2 placebo

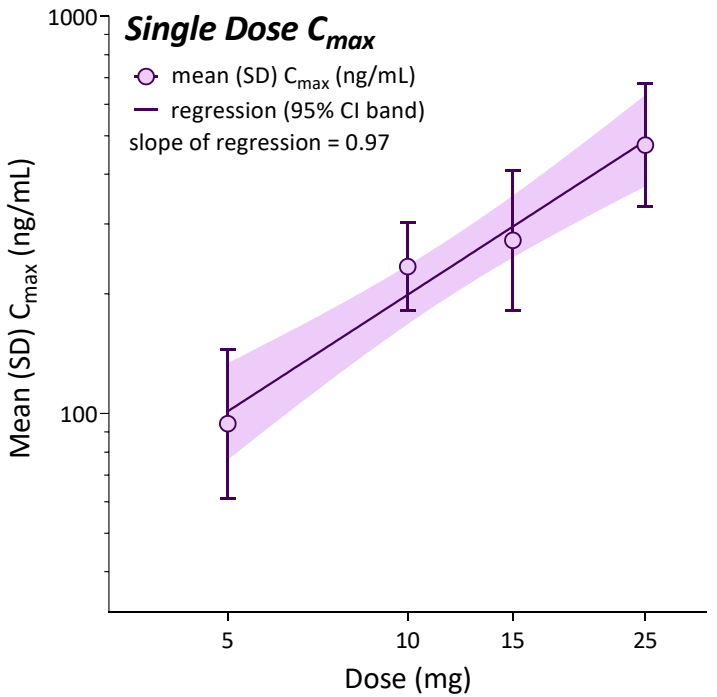
Dose levels evaluated:

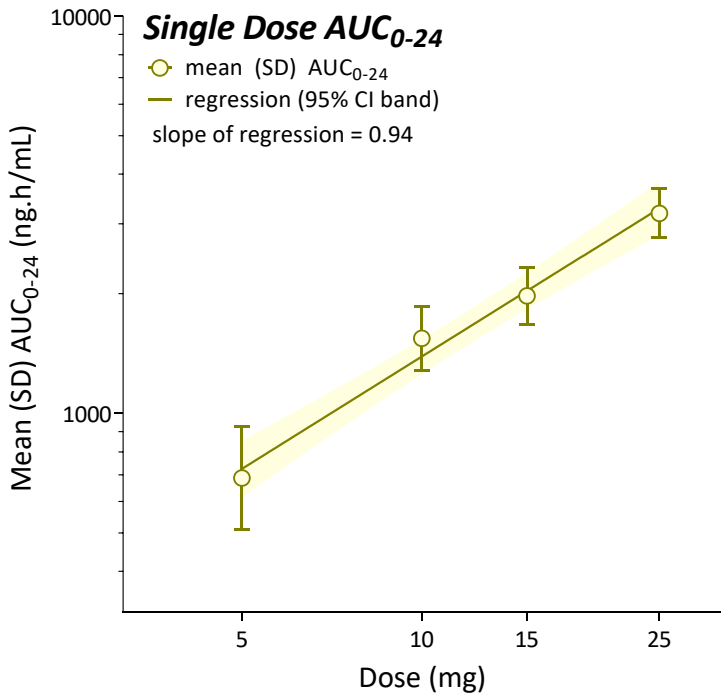
- 5mg
- 10mg
- 15mg
- 20mg

BCX9250 SAD PK Profile and Dose-exposure Analysis

BCX9250 exposure was approximately linear and dose proportional over the doses evaluated

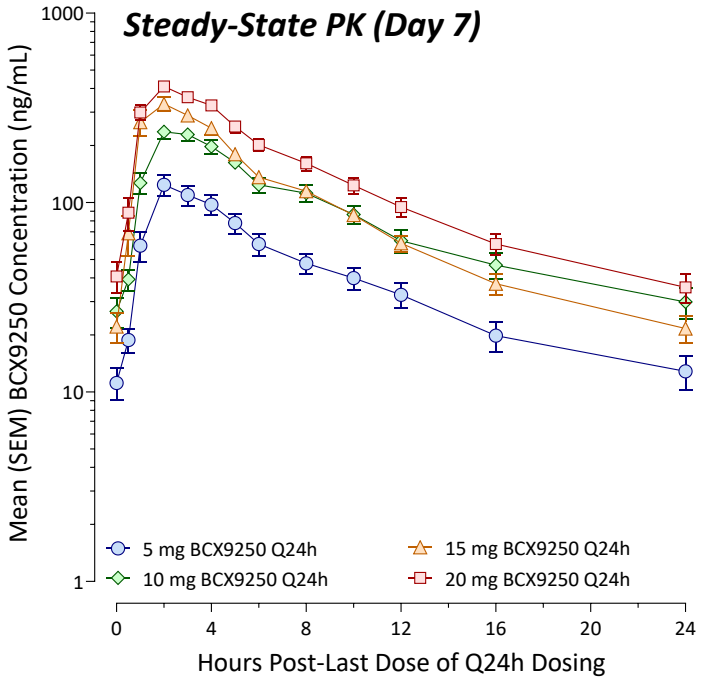


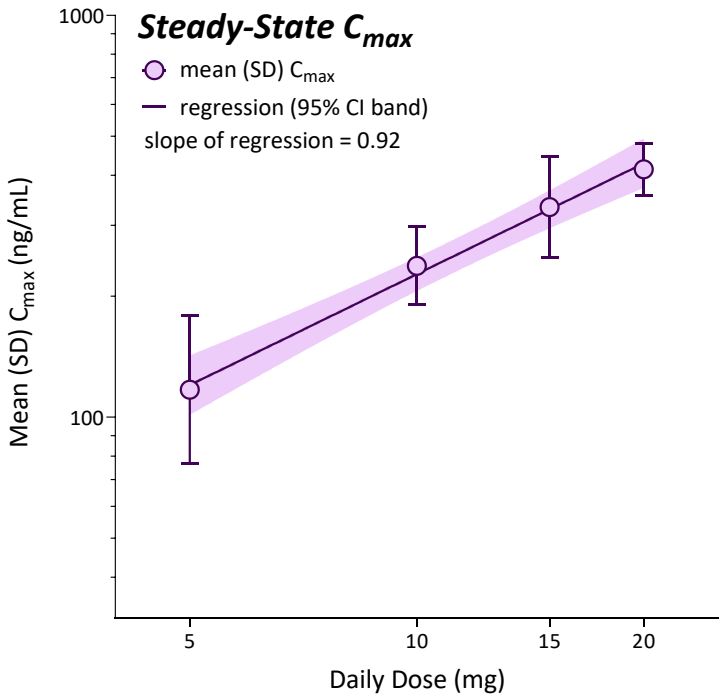


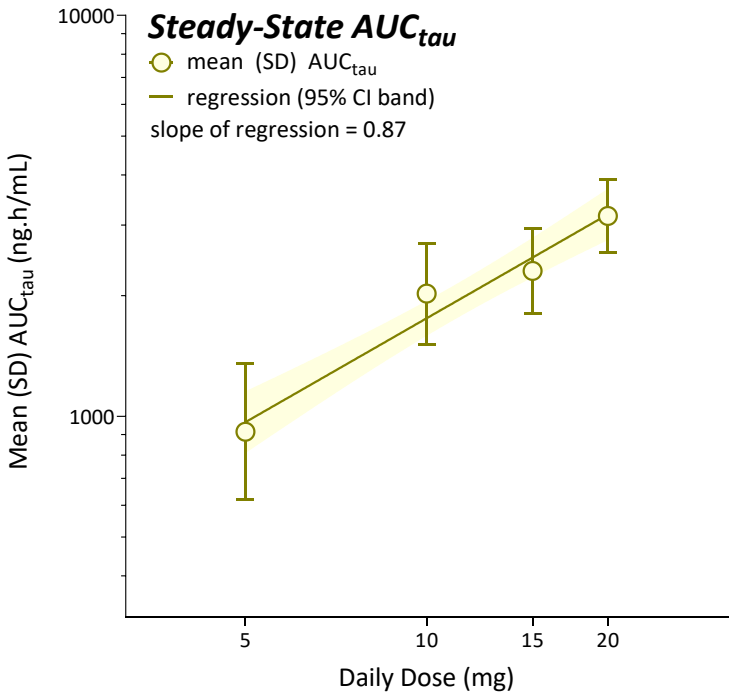


BCX9250 MAD PK Profile and Dose-exposure Analysis

BCX9250 steady-state exposure was approximately linear and dose proportional over the doses evaluated, with minimal accumulation relative to the first dose







BCX9250 Phase 1 Trial: Summary of Adverse Events

Category of Treatment-Emergent Adverse Event (TEAE)	Single Ascending Doses (SAD)						Multiple Ascending Doses (MAD)				
All data is reported as subject incidence, n (%)	**Placebo**	**BCX9250**					**Placebo**	**BCX9250**			
	(n=8)	**5 mg (n=6)**	**10 mg (n=6)**	**15 mg Fasted (n=6)[a]**	**15 mg Fed (n=6)**	**25 mg (n=6)**	**(n=7)[b]**	**5 mg (n=10)**	**10 mg (n=10)**	**15 mg (n=10)**	**20 mg (n=10)**
At least one TEAE	4 (50.0)	0	0	4 (66.7)	3 (50.0)	0	5 (71.4)	6 (60.0)	3 (30.0)	6 (60.0)	6 (60.0)
Drug-related TEAEs	3 (37.5)	0	0	2 (33.3)	0	0	4 (57.1)	0	3 (30.0)	1 (10.0)	0
Grade 3 or 4 TEAEs	0	0	0	0	0	0	0	0	0	0	0
Serious TEAE	0	0	0	0	0	0	0	0	0	0	0
Drug-related serious TEAE	0	0	0	0	0	0	0	0	0	0	0
TEAE leading to study discontinuation	0	0	0	0	0	0	0	0	0	0	0
Drug-related TEAE leading to study discontinuation	0	0	0	0	0	0	0	0	0	0	0
TEAEs reported by 2 or more subjects [c]											
Medical device site reaction [d]	0	0	0	2 (33.3)	1 (16.7)	0	0	2 (20.0)	0	1 (10.0)	3 (30.0)
Headache	2 (25.0)	0	0	1 (16.7)	0	0	1 (14.3)	0	2 (20.0)	2 (20.0)	0
Vessel puncture site pain	1 (12.5)	0	0	0	0	0	1 (14.3)	1 (10.0)	0	0	2 (20.0)
Abdominal discomfort	2 (25.0)	0	0	0	0	0	0	0	1 (10.0)	0	0
Abdominal pain	1 (12.5)	0	0	0	0	0	0	0	1 (10.0)	0	1 (10.0)
Diarrhea	1 (12.5)	0	0	0	0	0	0	0	2 (20.0)	0	0
Constipation	0	0	0	0	0	0	1 (14.3)	0	0	1 (10.0)	0
Flatulence	0	0	0	0	0	0	1 (14.3)	0	1 (10.0)	0	0
Nausea	1 (12.5)	0	0	1 (16.7)	0	0	0	0	0	0	0
Cough	1 (12.5)	0	0	0	0	0	0	0	1 (10.0)	0	0

[a] One subject discontinued from study after completing first dose (fasted) and was replaced for the second dose (fed).

[b] Only one placebo subject was enrolled in MAD 20 mg cohort. The last subject was not enrolled due to impact of COVID-19 on screening.

[c] All TEAEs were mild except for one event of moderate myalgia in the MAD 10 mg dose group, not related to study drug.

[d] Reported event: electrode site (skin) irritation due to ECG lead placement