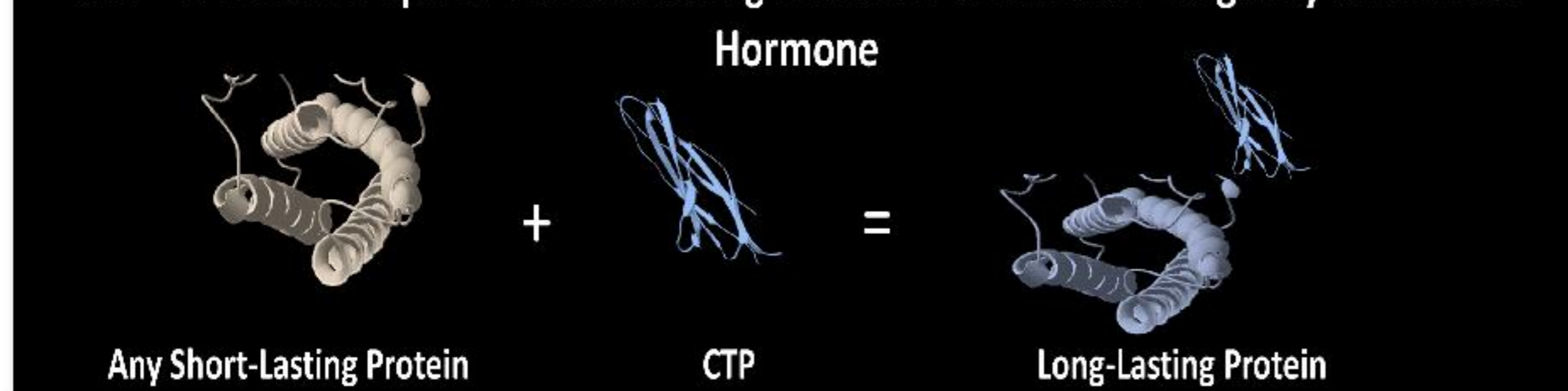


## Introduction

OPKO Biologics developing bio better long acting versions of existing therapeutic proteins utilizing a technology called CTP.

### CTP – A Natural Peptide Created During Evolution to Enhance Longevity of the hCG Hormone



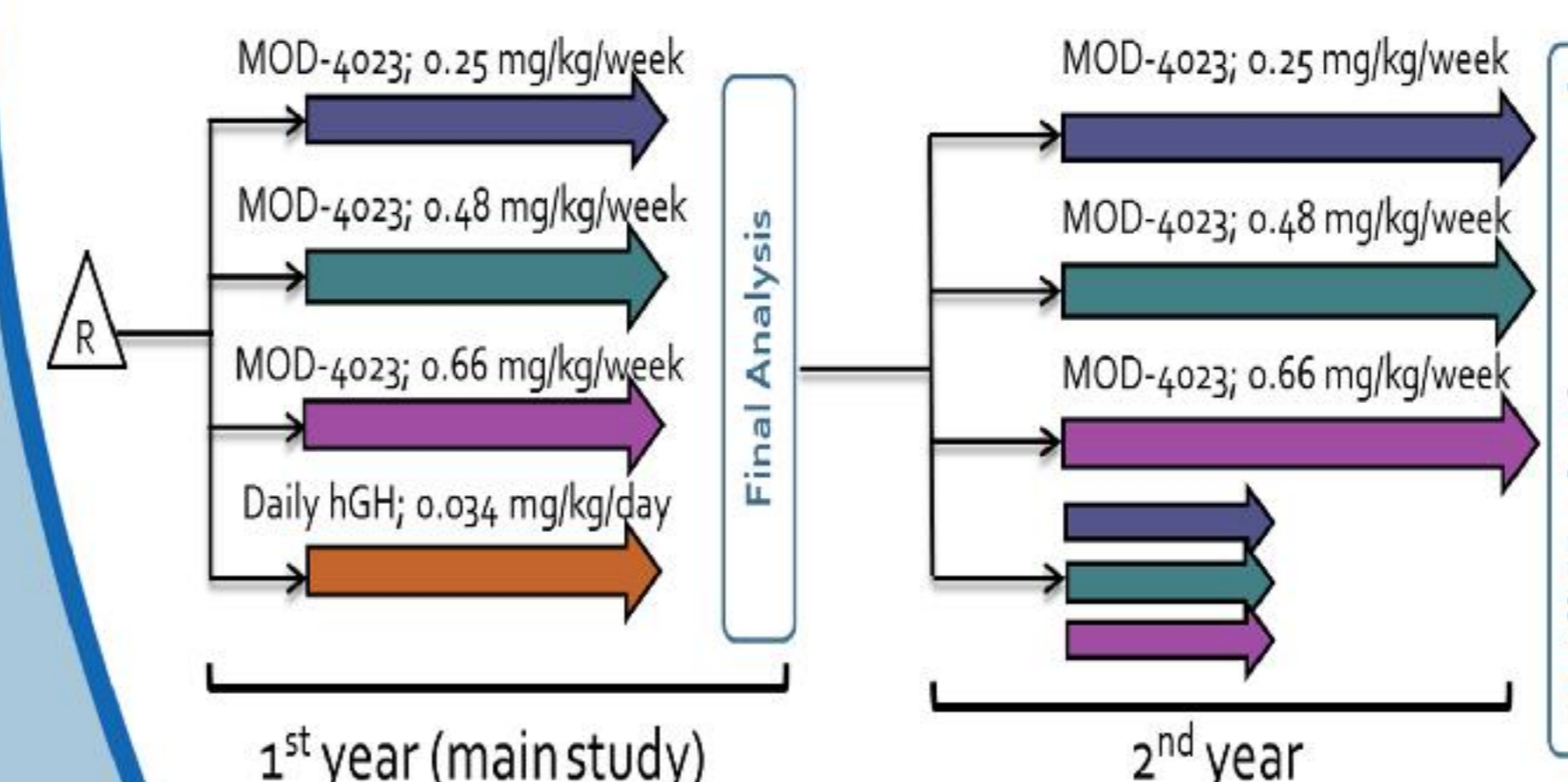
The technology involves fusion of the C terminus peptide of hCG to one or both ends of the target protein. The technology was clinically validated and proven as a safe and efficient way for increasing the half-life of several therapeutic proteins while maintaining their biological activity. MOD-4023 (hGH-CTP) is a long acting hGH with the following competitive advantages:

- Non Viscous, high concentration formulation
- Consists of ~75% native hGH content
- hGH-CTP is injected by pen device with 30 - 31G needle

## Study Outline

A one-year, randomized, comparator-controlled Phase 2 study that included 53 pre-pubertal GHD children with GHD was conducted. The patients received once-weekly SC injections of MOD4023 (0.25, 0.48, or 0.66 mg/kg/week), or daily hGH (34 µg/kg/day) as control. Forty-six Patients were rolled over to an open-label extension study (OLE) and continued to be administered with the same MOD-4023 dosages on a weekly basis, in order to assess longer-term safety and efficacy. Height velocity (HV) in 45 patients during the second year of MOD-4023 treatment was monitored and compared to historical controls (Ranke et al., 2010). IGF-1 and IGFBP-3 levels were monitored as well.

### Overall Study Design

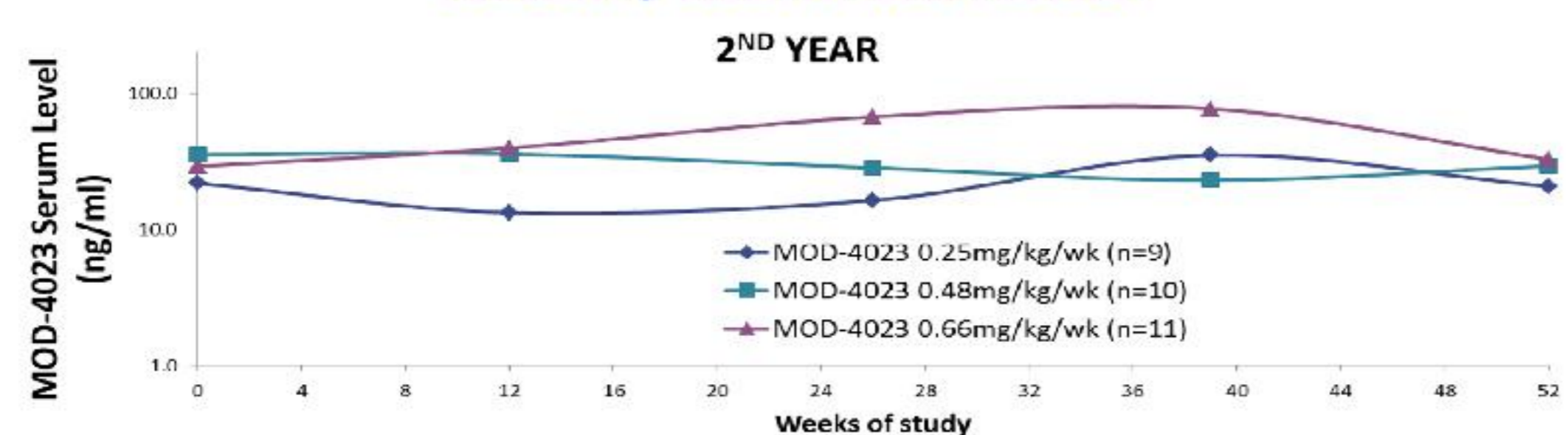


### Baseline Characteristics (n=52)

	Cohort 1 (n=13)		Cohort 2 (n=15)		Cohort 3 (n=13)		Cohort 4 (n=11)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age at V1	6.92	2.19	6.53	2.20	7.08	2.40	6.43	1.79
HT SDS	-3.64	0.97	-3.72	0.87	-4.21	1.45	-4.22	1.58
HT SDS - THSDS	-3.22	0.95	-3.00	0.70	-3.36	1.54	-3.68	1.70
HV SDS	-2.93	1.42	-2.68	1.00	-3.01	1.42	-3.29	1.91
Peak GH	3.93	3.15	4.13	2.64	3.97	2.97	3.82	2.78
SCREENING IGF-1 SDS	-2.13	0.85	-2.13	0.77	-1.97	0.83	-2.15	0.94

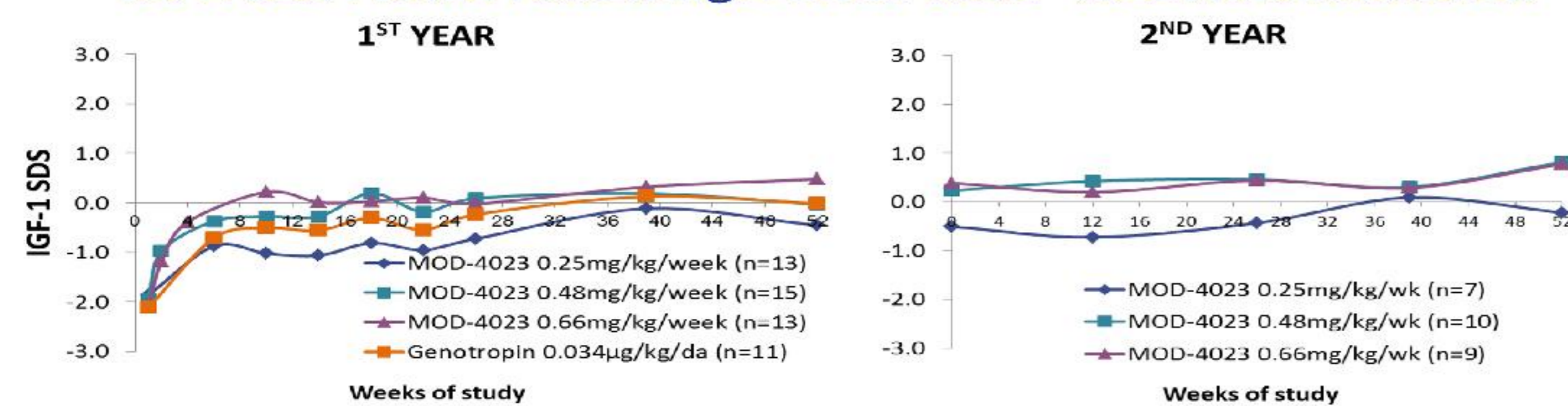
## PK / PD

### MOD-4023 Mean Serum Concentrations Following 24m of once-weekly administration

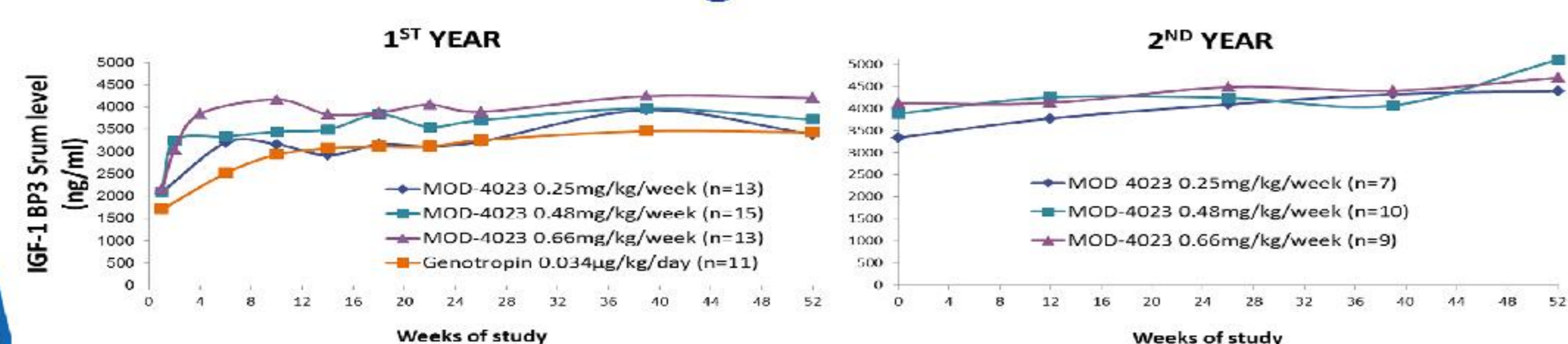


\* MOD-4023 samples were collected after 3-4 days from injection.

### IGF1-SDS Profile Following 24m of MOD-4023 Administration

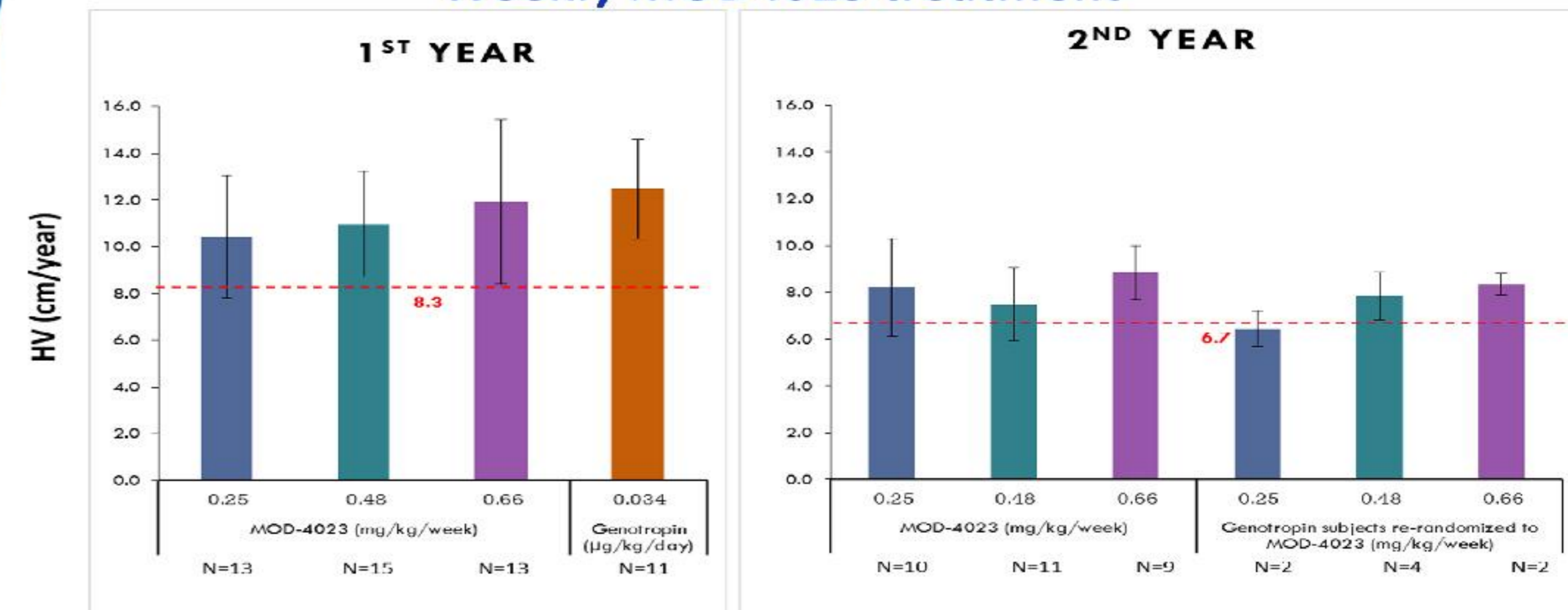


### IGF1-BP3 Profile Following 24m of MOD-4023 Administration

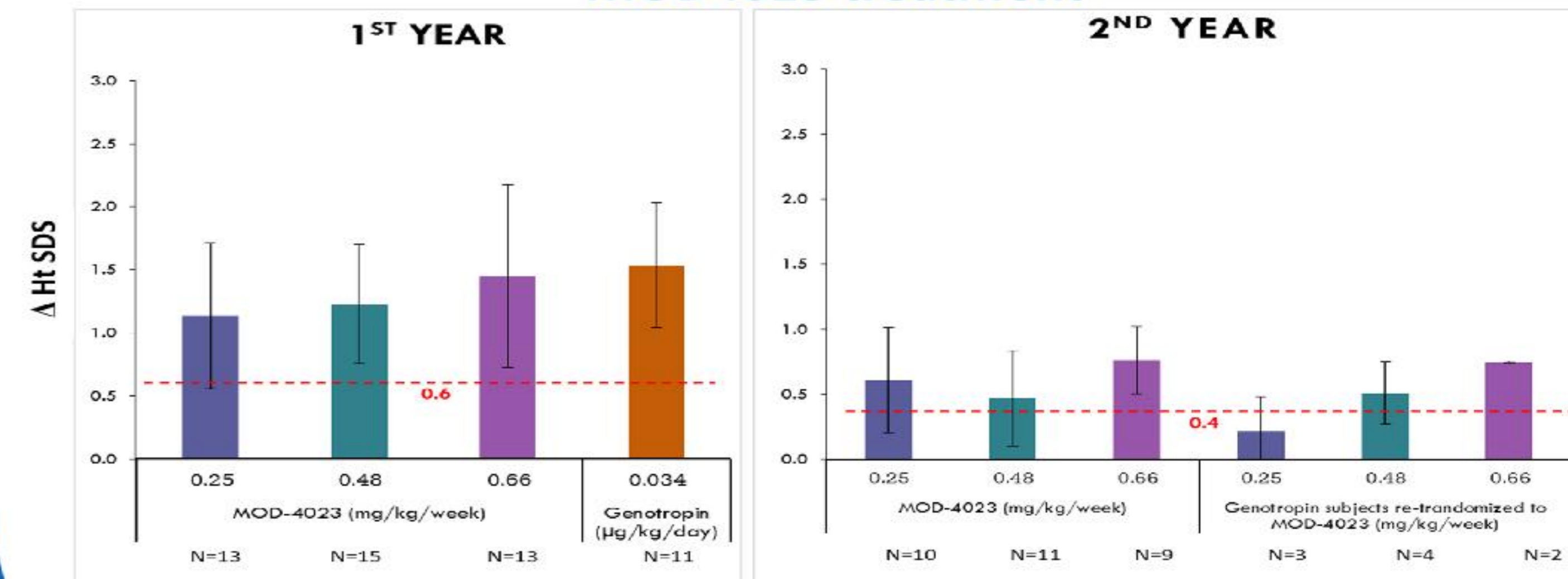


## Efficacy

### Mean Annualized HV for subjects completed 24m of Once-Weekly MOD4023 treatment



### Delta Height SDS for subjects completed 24m of Once-Weekly MOD4023 treatment



Clinical data. ©Ranke et al.  
\* Error bars indicate +/- 1SD

## Conclusions

- Weekly administration of MOD-4023 maintained a steady-state levels with no apparent significant increase in plasma level, which was measured on Day 4 post dosing over the 24m of study periods.
- MOD-4023 provided an adequate IGF1-SDS response, well within the normal range, reaching an optimal average value of 0 SDS, and most importantly, not exceeding +2 SDS on Day 4 post-dosing up to 24 months.
- IGFBP-3 also increased in a dose-dependent manner upon MOD-4023 administration, reaching steady-state values during the first and second year of the study.
- Efficacy data confirmed that single weekly administration of MOD-4023 for the treatment of pediatric GHD patients during 24m led to promising 2<sup>nd</sup> year growth, also when compared to pre-published GH clinical study (Ranke et al., 2010).
- To sum, the presented data further affirms that once-weekly injection of MOD4023 could replace daily injections of hGH in GHD children.

**The PK-PD, efficacy and safety data support the initiation of a Phase 3 study in GHD pediatric population using a single weekly injection of MOD-4023.**