

# Immunogenicity Results of Once-Weekly Administration of CTP-Modified Human Growth Hormone (MOD-4023): A Phase 2 Study in Children with Growth Hormone Deficiency

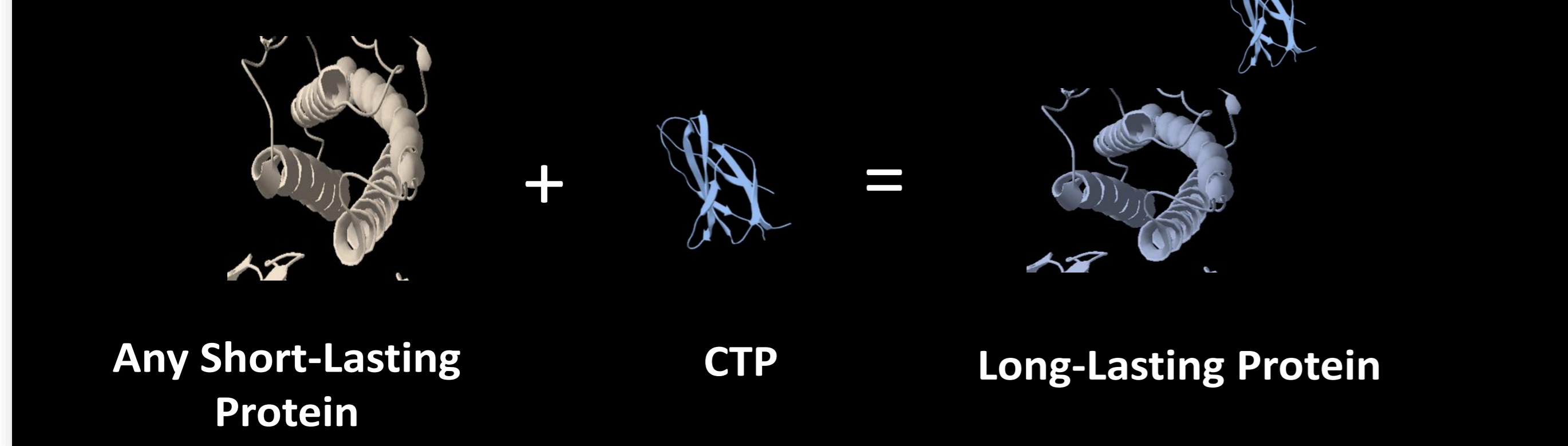
Michal Jaron-Mendelson, PhD, Ahuva Bar-Ilan, PhD, Oren Hershkovitz, PhD, Gili Hart, PhD  
OPKO Biologics, Nes Ziona, Israel

Disclosure statement: nothing to disclose.

## Introduction

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

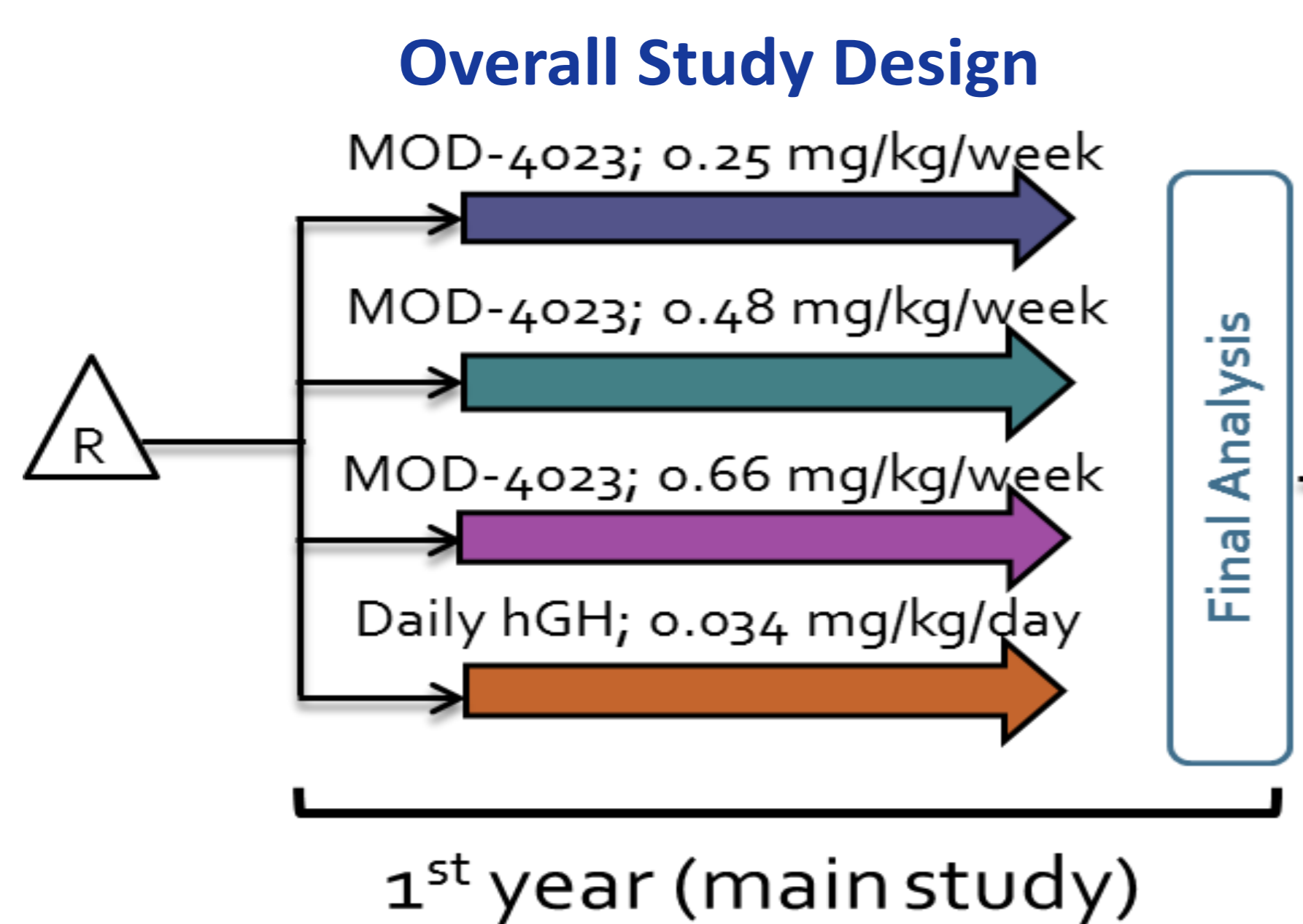
CTP – A Natural Peptide Created During Evolution to Enhance Longevity of the hCG Hormone



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

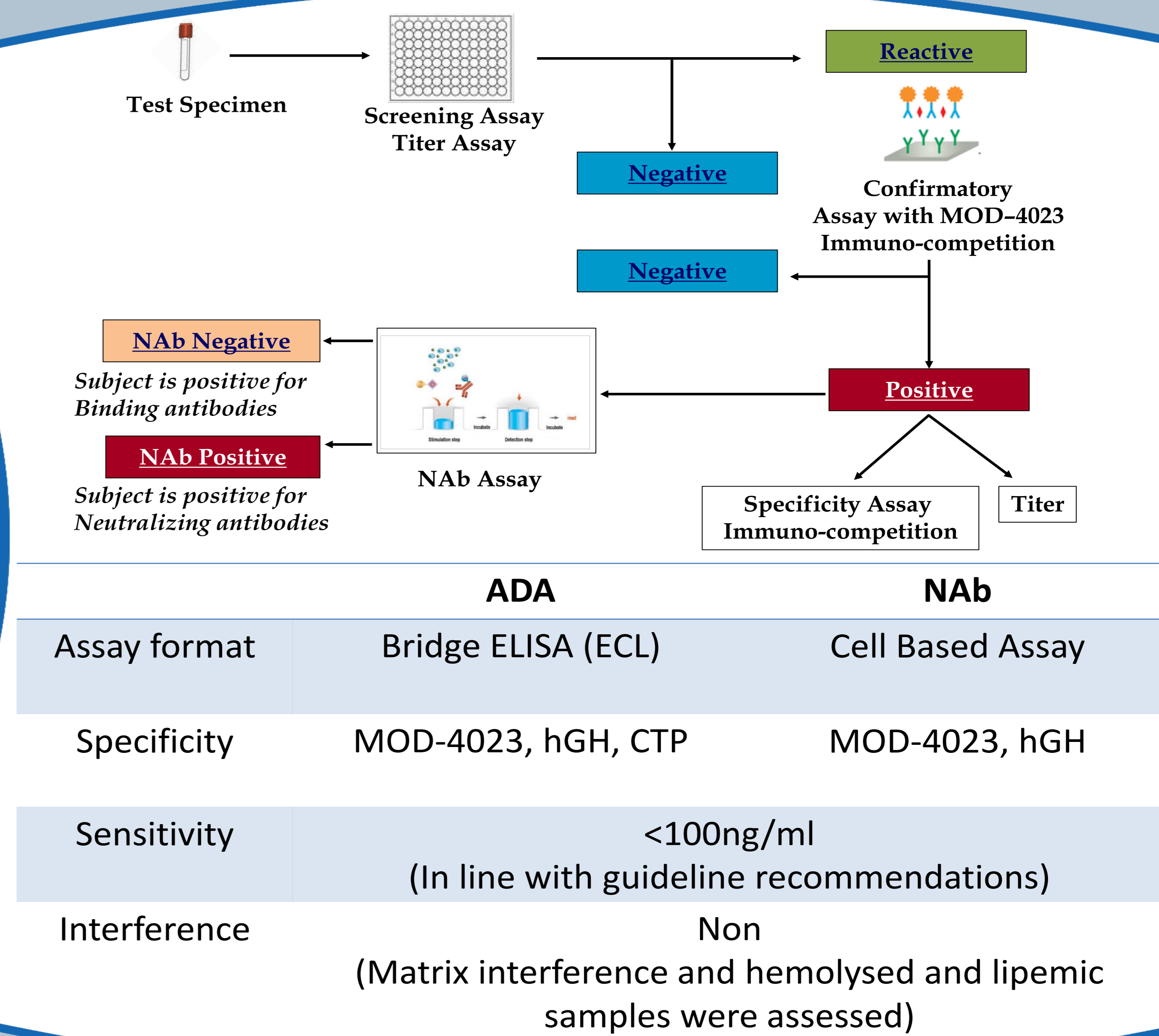
## Study Outline

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.



Serum samples for immunogenicity analysis were collected at pre-dose, and after 6 and 12 months of MOD-4023/ hGH treatment. Each sample was analyzed in screening format. Samples reactive for anti-MOD-4023 Ab's were confirmed for MOD-4023 in specificity format. Then, samples confirmed positive for anti-MOD-4023 binding Ab's, were titered and further characterized (anti CTP, anti GH), as well as for anti-MOD-4023 and anti-hGH neutralizing Ab's using cell-based assays.

## Immunogenicity Paradigm



## Results

Cohort	Incidence (12 months)
<b>ADA</b>	
MOD-4023 0.25 mg/kg/wk	0/13
MOD-4023 0.48 mg/kg/wk	3/15
MOD-4023 0.66 mg/kg/wk	2/14
<b>MOD-4023 treatment (Total)</b>	<b>11.4% (5/42)</b>
<b>Genotropin treatment (0.034 µg/kg/day)</b>	<b>9% (1/11)</b>
<b>NAb</b>	
<b>Total</b>	<b>0/53</b>

- A comparable rate of ADAs between MOD-4023 and Genotropine treatment arms.
- Low Ab titers found for the Positive subjects to ADA.
- Non of the ADAs were specific to the CTP portion, meaning that CTP had no immunogenic affect.
- No neutralized anti-MOD-4023 or hGH Abs.
- No AE's which are Abs related were reported.
- No effect on PK/PD (IGF-1) nor on HV were observed.

## Conclusions

- Precise, sensitive and reproducible qualitative methods were validated for the detection of binding as well as neutralizing Ab's, against MOD-4023 and it's moieties; hGH and CTP.
- During the first 12 months of the Phase 2 study in GHD pediatric population, MOD-4023 has demonstrated a comparable immunogenicity profile to the observed (as well as reported; Peter et al 2013) with daily administrated hGH.
- The data affirms that a single weekly injection of MOD-4023 has the potential to safely replace the daily hGH injections in children with GHD.

**The Immunogenicity data support the initiation of a Phase 3 study in GHD pediatric population using a single weekly injection of MOD-4023.**

