Subject: Competitive Intelligence - SciWind Oral GLP1 (XW-004)
Date: Wednesday, January 24, 2024 at 11:11:26 AM Eastern Standard Time
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Hi All,

SciWind just reported positive Phase 1 MAD data for XW-004, an oral tablet formulation of ecnoglutide. Highest dose showed 5.9% placebo-adjusted weight loss at week 6.

For reference, ecnoglutide is an injectable biased GLP1R agonist developed for T2DM and Obesity. Ecnoglutide is currently in Phase 3 T2DM study and Phase 2 Obesity study in China.

Key takeaways include:

- 6-week MAD study is Australia-based (NCT05184322)
- 56 patients (42 healthy, 14 obese) were enrolled across 4 cohorts
  - Cohorts 1-3 received 7, 15, or 30 mg dose once-daily for 2 weeks
    - Cohorts 1, 2 started on 2 mg dose, up-titrate every 5 days to 7 mg, then 15 mg (cohort 2 only)
    - Cohorts 3 started on 7 mg dose, up-titrate every 5 days to 7, 15, and 30 mg
  - Cohort 4 received 30 mg dose, once-daily for 6 weeks
    - Cohort 4 started on 2 mg dose, up-titrate every 5 days to 7, 15, and 30 mg
- 5.9% placebo-adjusted weight loss (6.8% total weight loss) at week 6 was observed in Cohort 4, which received highest dose
  - Cohorts 1-3 had placebo-adjusted weight loss of 2.9%, 2.7%, and 5.9% (placebo weight loss is 0.9%) at week 2
- Study is ongoing, evaluating once-weekly oral administration.

Interesting to see if once-weekly oral administration is possible. Oral peptide space is heating up!

Best,
Jay

Sciwind Biosciences Announces Positive Results from Phase 1 Clinical Trial of XW004, an Oral Formulation of Long-acting GLP-1 Analog Ecnoglutide

NEWS PROVIDED BY
Hang Zhou Sciwind Biosciences Co., Ltd.
23 Jan, 2024, 21:00 ET
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- *Oral ecnoglutide was safe and well tolerated with gastrointestinal side effects as the most commonly reported adverse events*
- *Study participants receiving up to 30 mg oral ecnoglutide once-daily for 6 weeks achieved a mean body weight reduction of -6.8% from baseline, compared to -0.9% for the placebo group*
- *The study remains ongoing to evaluate additional dosing regimens including once-weekly oral administration*

HANGZHOU, China and SAN FRANCISCO , Jan. 23, 2024 /PRNewswire/ -- Sciwind Biosciences Co., Ltd., a clinical-stage biopharmaceutical company focused on discovering and developing innovative therapies to treat metabolic diseases, today announced positive interim results from the first four cohorts of a Phase 1 clinical trial of oral ecnoglutide (XW004). Ecnoglutide is a long-acting, cAMP signaling biased, glucagon-like peptide-1 (GLP-1) analog that is being developed for the treatment of type 2 diabetes and obesity. XW004 is an oral tablet formulation of ecnoglutide.

The Phase 1 trial (NCT05184322) is a randomized, double-blind, placebo-controlled multiple ascending dose study that enrolled 42 healthy (Cohorts 1-3) and 14 healthy obese (Cohort 4) participants in Australia. Participants were randomized to receive placebo or XW004 as once-daily oral tablets. In Cohorts 1-3, target doses were 7 mg, 15 mg, or 30 mg XW004 once-daily for 2 weeks; in Cohort 4 the target dose was 30 mg XW004 once-daily for 6 weeks. Treatment periods included gradual dose escalation to the target doses. Safety, tolerability, pharmacokinetics and changes in mean body weight from baseline were evaluated.

Overall safety and tolerability of oral ecnoglutide were consistent with the established profile of GLP-1 peptide agonists. The most frequently reported adverse events included nausea, headache, diarrhea, vomiting, and decreased appetite. The majority of adverse events were mild to moderate in severity and occurred mostly during the dose-escalation periods.

At baseline, participants had a mean body weight of 75.6 to 77.9 kilograms for Cohorts 1-3 and 100.1 kilograms for Cohort 4. Mean BMI at baseline was 25.8 to 26.1 kg/m^2 for Cohorts 1-3 and 32.9 kg/m^2 for Cohort 4. In Cohorts 1-3, treatment with doses up to 7, 15, or 30 mg XW004 once-daily for 2 weeks resulted in body weight changes of -3.6%, -3.4%, and -6.6%, respectively, compared to -0.9% for the placebo group. In obese participants (Cohort 4), treatment with doses up to 30 mg XW004 once-daily for 6 weeks resulted in -6.8% body weight loss at end of treatment, compared to -0.9% for the placebo group. In addition, pharmacokinetics of XW004 showed good absorption after oral administration.

Table. Summary of mean body weight changes from baseline in Cohorts 1-4			
		Body weight change from baseline (%)	
Study Cohort	XW004 dosing schedule (once daily)	Week 2	Week 6
Placebo (N=8)	N/A	-0.9 %	-0.9 %
Cohort 1 (N=10)	2mg (day 1-5) -> 7mg (day 6-15)	-3.6 %	N/A
Cohort 2 (N=10)	2mg (day 1-5) -> 7mg (day 6-10) -> 15mg (day 11-15)	-3.4 %	N/A
Cohort 3 (N=11)	7mg (day 1-5) -> 15mg (day 6-10) -> 30mg (day 11-15)	-6.6 %	N/A
Cohort 4 (N=11)	2mg (day 1-5) -> 7mg (day 6-10) -> 15mg (day 11-15) -> 30mg (day 16-44)	-2.5 %	-6.8 %

"We are very encouraged by the favorable safety, efficacy, and pharmacokinetic profile of XW004 observed in this study. The strong body weight loss results after short-term administration support the development of oral ecnoglutide for the treatment of obesity and type 2 diabetes" said Hai Pan, founder and CEO of Sciwind Biosciences.

Based on the results of Cohorts 1-4, the study is continuing and will evaluate additional dosing regimens, including once-weekly oral administration of XW004 in participants with obesity. "We believe that less frequent dosing regimens can significantly improve patient compliance, overcome manufacturing challenges, and greatly increase access to this drug class for broad patient populations," said Mohammed Junaidi, MD, Sciwind Vice President of Clinical Development. "If successfully developed, XW004 has the potential to become the first once-weekly oral GLP-1 receptor agonist for the treatment of metabolic conditions."

About ecnoglutide (XW003 and XW004)

Glucagon-like peptide-1 (GLP-1) analogs are effective therapies in managing type 2 diabetes, obesity, and have demonstrated clinical potential as a treatment for NASH. Ecnoglutide (XW003) is a novel, cAMP signaling biased, long-acting GLP-1 analogue optimized for improved biological activity, cost-effective manufacturing, and once weekly dosing. XW003 has demonstrated treatment benefits for patients with type 2 diabetes and obesity and is safe and well tolerated in clinical studies. XW004 is an oral tablet formulation of ecnoglutide.

About Sciwind

Sciwind Biosciences is a clinical stage biopharmaceutical company focusing on discovering and developing innovative therapies to treat metabolic disease. Its product pipeline consists of potentially first-in-class and best-in-class drug candidates, including the long-acting GLP-1 peptide analog ecnoglutide (Phase 3), oral ecnoglutide tablet XW004 (Phase 1), and oral small molecule GLP-1 receptor agonist XW014 (Phase 1). Sciwind has developed multiple proprietary technologies, including oral peptide and inhaled protein therapeutic delivery platforms and identified a series of drug candidates based on these core platform technologies. For more information, visit **www.sciwindbio.com**.

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