Uni-Bio Science Group Ltd.
聯康生物科技集團有限公司*

*(Incorporated in the Cayman Islands with limited liability)*

**(Stock code: 0690)**

# VOLUNTARY ANNOUNCEMENT
# RESULTS OF PHASE III UNI-E4 CLINICAL TRIAL

## I. IMPORTANT NOTICE

1. Reference is made to the announcement ("Announcement") of Uni-Bio Science Group Limited (the "Company"), together with its subsidiaries, (the "Group") dated 21 March 2014. Unless otherwise specified, terms used herein shall have the same meaning as those defined in the Announcement.

2. Information disclosed in this announcement is the results of the efficacy analysis from the clinical trial entitled Recombinant Exendin-4 Phase III Clinical Trial ("Uni-E4 Clinical Trial"). The Group's Recombinant Exendin-4 ("Uni-E4") is a prescription new drug for treating Type 2 diabetes. The statistical results disclosed of this announcement were provided to the Group by an independent statistical group as of the date of this announcement.

3. This announcement is prepared in both English and Chinese. In the event of discrepancy, the Chinese version shall prevail.

## II. EXECUTIVE SUMMARY OF UNI-E4 CLINICAL TRIAL

### 1. Background

Type 2 diabetes mellitus ("T2D") is a clinical syndrome, characterized by hyperglycemia, affecting over 100 million people in China. With rising prevalence and an aging population, there is a great demand for newer, safer and more cost-effective therapeutics.

Uni-E4, a recombinant version of Glucagon-like Protein-1 ("GLP-1") receptor agonist, lowers blood glucose level through stimulating insulin production, as well as inhibiting glucagon release. Distinguished from other T2D treatments, it effectively leads to weight loss and lower risk of hypoglycemia; two clinical advantages very important in managing T2D complications in the long term. Uni-E4 has the potential to address unmet clinical needs as a cost-effective treatment option for Chinese T2D patients, especially those who are also overweight (a sub-population representing 30% of the total T2D patients).

* *For identification purpose only*

## 2. Method

A 24-week randomized, open-label, parallel-group, multi-center, non-inferiority trial design was implemented to evaluate the efficacy and safety of Uni-E4 versus the positive control group of insulin glargine in treating T2D. The primary efficacy endpoint was the change of Glycosylated Hemoglobin ("HbA1c") after 24 weeks of treatment; secondary efficacy endpoints included, but were not limited to, the proportion of patients achieving HbA1c of ≤7% and ≤6.5%, and change in body weight with safety being evaluated in parallel. A total of 471 patients were enrolled with written informed consent and randomized in a 3:1 ratio to receive Uni-E4 (treatment group, n=355) or insulin glargine (control group, n=116). The Uni-E4 clinical trial was led by the Second Xiangya Hospital of Central South University with the participation of 12 other hospitals. Statistical analysis was performed by the Department of Health Statistics, Second Military Medical University. HbA1c and other biomarkers were measured by the Shanghai First People's Hospital.

## 3. Clinical Trial Objectives

In a Phase II trial led by the Group, Uni-E4 was successfully shown to decrease HbA1c in patients with T2D after 12 weeks of treatment. Based on the Phase II trial results, the objective of the Phase III trial was to further evaluate the efficacy and safety of Uni-E4 in treating T2D. The results will be reviewed by China Food and Drug Administration ("CFDA") for New Drug Application ("NDA").

## 4. Clinical Study Results

### *4.1 Patient baseline comparability*

Patients in the treatment and control group had similar demographic characteristics, vital signs, medical history and results of blood biochemical test, blood routine examination and urine routine examination at baseline. There were no statistically significant differences (P>0.05), therefore the two groups were comparable.

### *4.2 Clinical results**

| Endpoint | Type | Observation time | Trial group (n=348) | Control group (n=115) | Statistical results of the two groups |
|---|---|---|---|---|---|
| Change of HbA1c | Primary efficacy endpoint | After 24 weeks of treatment | 8.41% (before treatment) to 7.39% (after treatment), with an average decrease of 1.02% | 8.42% (before treatment) to 7.49% (after treatment), with an average decrease of 0.93% | No significant difference (P>0.05) |
| Proportion of patients achieving HbA1c ≤7% | Secondary efficacy endpoint | After 24 weeks of treatment | 38.79% | 34.78% | No significant difference (P>0.05) |
| Proportion of patients achieving HbA1c ≤6.5% | Secondary efficacy endpoint | After 24 weeks of treatment | 25.57% | 22.61% | No significant difference (P>0.05) |
| Change of body weight | Secondary efficacy endpoint | After 24 weeks of treatment | Decrease of 0.70 kg | Increase of 0.74 kg | Significant difference (P<0.05) |
| Rate of adverse events | Primary safety endpoint | After 24 weeks of treatment | 47.99% | 49.57% | No significant difference (P>0.05) |
| Rate of hypoglycemic reactions | Safety endpoint | After 24 weeks of treatment | 1.44% | 5.22% | Significant difference (P<0.05) |

*Note:* * The efficacy endpoints use FAS analytic set, while the safety endpoints use SS analytic set.

### *4.3 Safety*

The incidence of Adverse Events ("AEs") was consistent with the data reported in literature. Most common AEs included allergic reaction, dizziness, nausea, hypoglycemic reaction and rash.

## 5. Conclusion

The Phase III clinical trial results confirm that Uni-E4 is safe and efficacious in patients with T2D. Uni-E4 met its primary efficacy endpoint of HbA1c reduction after 24 weeks of treatment versus insulin glargine. In addition to lowering blood glucose level in patients with T2D, Uni-E4 can also decrease the body weight of patients and the incidence of hypoglycemic reactions, bringing more clinical benefits to the patients. Finally, Uni-E4 continues to exhibit a safe AE profile, consistent with past trials or that of similar drugs.

T2D is a clinical syndrome caused jointly by genetic and environmental factors, which is characterized by hyperglycemia and accompanied by metabolic disorders of fat, protein, water and electrolyte. The pathogenesis mainly include reduction of insulin production caused by the hypofunction of pancreatic islet beta cells and the body's lower sensitivity to insulin due to insulin resistance. Uni-E4 is a biological analogue of GLP-1, an incretin hormone; studies have shown that Uni-E4 can significantly stimulate insulin secretion, protect the functions of pancreatic islet beta cells and improve the body's sensitivity to insulin, resulting in lower fasting and postprandial plasma glucose levels. HbA1c is an important index to monitor blood glucose level, commonly used to reflect a patient's average glucose control over the past 12 weeks. Healthy people have HbA1c levels ranging from 4% to 6%, whereas diabetes patients have levels greater than 6.5%. In the Phase III trial, patients showed a strong decrease in HbA1c levels after 24 weeks of treatment, which demonstrates the effectiveness of Uni-E4 in blood glucose control.

It is known that obesity is an important factor that can lead to insulin resistance in diabetes patients and many antidiabetic drugs, including insulin, can contribute to increase in body weight, making further treatment even more difficult. Uni-E4 can effectively decrease the body weight of diabetes patients through suppressing the appetite and prolonging gastrointestinal emptying time. The results from the Phase III trial demonstrate that Uni-E4 can significantly decrease the body weight of diabetes patients when compared to insulin glargine. It indicates that Uni-E4 can improve the body's sensitivity to insulin through weight loss and bring further clinical benefits to the patients.

Hypoglycemic reactions are characterized by low blood glucose level, accompanied by clinical symptoms such as hunger, diaphoresis, anxiety, agitation and palpitation. It can aggravate vascular impairment in the patients and even endanger their lives. Many existing antidiabetic drugs can lead to a higher rate of hypoglycemic reactions, while they lower the blood glucose level in the patients. The harm caused by such blood glucose fluctuation in patients far outweighs the benefits brought by blood glucose control. For example, blood glucose fluctuation can increase the rate of hypoglycemia reactions, resulting to higher death rate in the patients. However, Uni-E4's action on receptor stimulation is glucose-dependent: when blood glucose level drops below a certain level, the up-regulatory effect on insulin secretion by Uni-E4 is decreased, thus lowering the risk of hypoglycemia. The clinical trial results show that compared to insulin glargine (5.22%), Uni-E4 can lead to a lower rate of hypoglycemia reactions (1.44%). In addition, Uni-E4 showed a lower rate of hypoglycemia reactions when compared with that of other antidiabetic drugs (2.14%-18.89%)**. Therefore, Uni-E4 is not only able to effectively keep blood glucose level steady and decrease blood glucose fluctuation, but also lower the rate of diabetes complications in the long-run.

In summary, the results announced today demonstrate that Uni-E4 has the potential to help patients control their blood glucose, improve insulin resistance, as well as, better stabilize blood glucose levels. Furthermore, Uni-E4 can ameliorate body weight increase and hypoglycemia reactions caused by most antidiabetic drugs, bringing more long-term clinical benefits to patients.

## III. THE GROUP'S NEXT ARRANGEMENTS

The Group plans to finalize the clinical trial summary report of the Uni-E4 clinical trial and submit a NDA to the CFDA in early 2016.

## IV. RISK WARNINGS

The Group plans to submit the NDA to the CFDA in early 2016. Should CFDA require the Group to provide supplemental research data, this may lead to extension of the time required for approval.

The results of the Uni-E4 clinical trial do not automatically mean an approval from the CFDA will be granted. The approval of Uni-E4 is subject to the final decision of the CFDA.

***Remarks:*

*The above-mentioned rate of hypoglycemia reactions comes from the data of exenatide, metformin, repaglinide and gliclazide, collected by the Food and Drug Administration ("FDA") and other sources (both domestic and international). Please note that the clinical trial designs may differ from that of Uni-E4 and data from such trials may not be directly comparable*

By Order of the Board
**Uni-Bio Science Group Limited**
**Tong Kit Shing**
*Chairman*

Hong Kong, 3 August 2015

*As at the date of this announcement, the Board comprises two executive Directors, namely, Mr. Tong Kit Shing (Chairman) and Mr. Kingsley Leung; one non-executive Director, namely, Mr. Fung Kwok Leung; and three independent non-executive Directors, namely, Mr. Tsao Hoi Ho, Terry, Dr. Carl Aslan Jason Morton Firth and Mr. Zhao Zhi Gang.*