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## CHINA MEDICAL SYSTEM HOLDINGS LIMITED

康哲藥業控股有限公司\*

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

(Stock Code: 867)

### **Inside Information**

**and**

### **Resumption of Trading in Shares**

#### **I. Important Notice**

1. This announcement is made pursuant to Rule 13.09 of the Rules Governing the Listing of Securities (the “Listing Rules”) on The Stock Exchange of Hong Kong Limited (the “Stock Exchange”) and the Inside Information Provisions (as defined under the Listing Rules) of Part XIVA of the Securities and Futures Ordinance (Chapter 571 of Laws of Hong Kong) by China Medical System Holdings Limited (the “Company” or “CMS”), along with its subsidiaries (the “Group”).

2. Information disclosed in this announcement is the preliminary results of the efficacy analysis from the clinical trial entitled “A Randomized, Double-Blind, Placebo-Controlled, Multicenter Phase III Study to Evaluate the Safety and Efficacy of Tyroserleutide for Injection in the Patients with Hepatocellular Carcinoma” (CMS024 Clinical Trial). Tyroserleutide (CMS024) for injection is a National Class 1.1 New Drug developed by the Group. The statistical results disclosed of this announcement were provided to the Company by an independent statistical group as of the date of this announcement.

3. At the request of the Company, trading in the shares of the Company on the Stock Exchange has been suspended since 9:00 a.m. on 3 March 2014 pending the release of this announcement. The Company has made an application to the Stock Exchange for the resumption of trading in the shares of the Company on the Stock Exchange with effect from 9:00 a.m. on 5 March 2014.

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

## **II. Executive Summary of CMS024 Clinical Trial**

### **Background:**

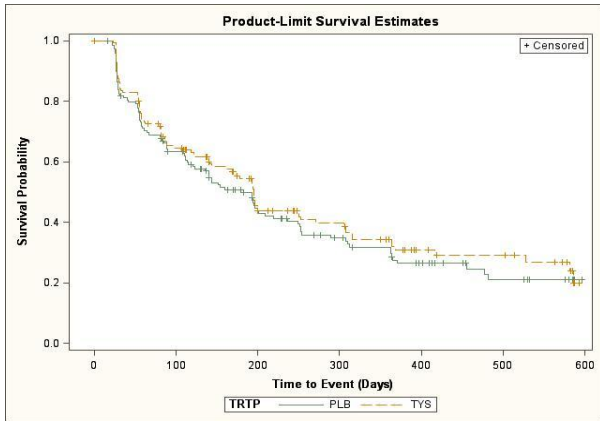
Zhongshan Hospital affiliated to Fudan University was the leading principal investigator of the clinical trial. Additional 23 clinical sites participated, including Eastern Hepatobiliary Surgery Hospital, West China Hospital Sichuan University and Tongji Medical College Huazhong University of Science and Technology Wuhan Union Hospital, etc. Medpace Inc. (USA) and the Clinical Research Institute of Peking University worked together to perform monitoring, data management and statistical analysis of the clinical trial. The entire database is stored in the server at Medpace Inc. (USA). The international Good Clinical Practice (GCP) standards were strictly followed.

This was a randomized, double-blind, placebo-control, multicenter study to evaluate the efficacy and safety of Tyrosuleutide for injection used to treat hepatocellular carcinoma. This study employed portal vein intra-abdominal chemotherapy with Fluorouracil (40ml) and Mitomycin (10mg) as a basal treatment in both treatment groups. The primary efficacy parameter was the recurrence-free survival (RFS) and the secondary efficacy parameter was the overall survival (OS). Interactive Voice/Web Response System (IVRS/IWRS) was employed in the randomization process, stratified by tumor invasion (yes/no, branches of portal vein involved by the tumor) and number of tumors (single/multiple) to ensure the balance at baseline. Statistical Analysis Plan (SAP) also pre-specified the subgroup analysis based on these two factors.

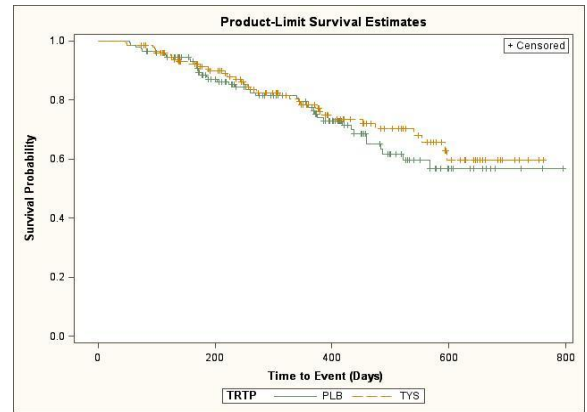
CMS024 Clinical Trial enrolled the first subject on 11 November 2011 and completed the enrollment of 300 subjects on 23 October 2013. The database was locked on 25 February 2014. In the afternoon of 28 February, at Shanghai Regal International East Asia Hotel, main principal investigators, clinical experts, statistical experts, sponsor and clinical research organization participated the blind data review of CMS024 Clinical Trial, followed by unblinding the database and preliminary statistical analysis.

### **Main Results of Efficacy Analysis:**

1. In the Full Analysis Set (FAS) (n=298), there is no statistically significant difference in the primary efficacy parameter RFS between the treatment and placebo groups ( $p=0.40$ ). For the secondary efficacy parameter OS, the difference between the two groups is not statistically significant ( $p=0.58$ ). Please see Figures 1.1 (RFS) and 1.2 (OS):

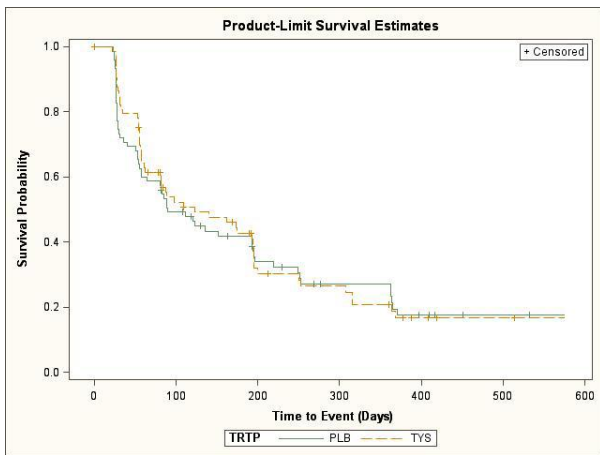


(Figure 1.1)

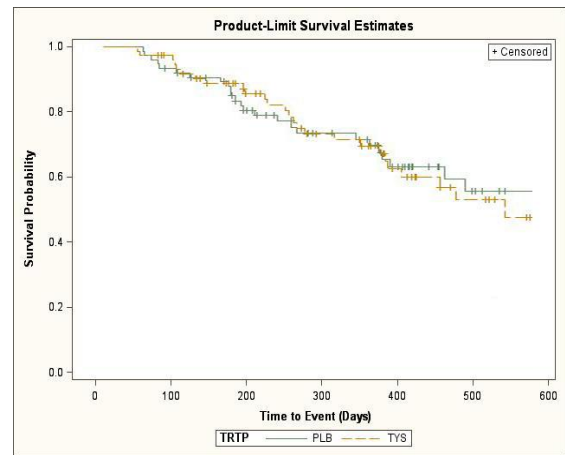


(Figure 1.2)

2. The subgroup analysis on subjects with tumor invasion (n=149) reveals that the survival curves of the treatment group and placebo group generally overlap with each other for both RFS and OS. Please see figures 2.1 and 2.2:

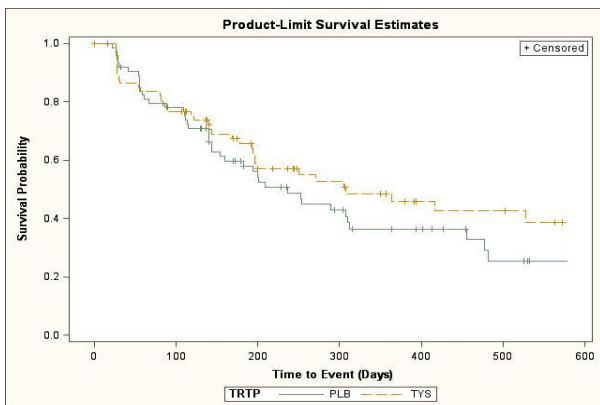


(Figure 2.1)

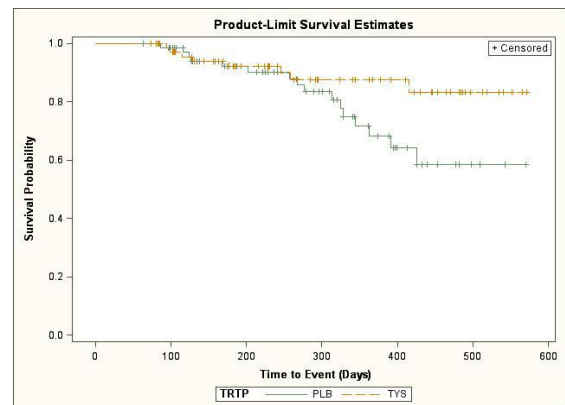


(Figure 2.2)

3. The subgroup analysis on subjects with no tumor invasion (n=149) reveals that there are favorable trends for the treatment group compared to the placebo group in both RFS and OS. Please see Figures 3.1 and 3.2:



(Figure 3.1)



(Figure 3.2)

### Subgroup Analysis:

1. There are notable differences in relapse rates between the tumor invasion subgroup and no tumor invasion subgroup.

There are a total of 298 subjects in FAS in the CMS024 Clinical Trial, with 149 subjects in each of the subgroup (with and without tumor invasion). “Tumor invasion” refers to the condition where the blood vessels have been seriously invaded by tumor, and is generally considered poor prognosis in the medical field, while conditions with no tumor invasion are with better prognosis. The data showed that the placebo group (n=75) with tumor invasion has a median RFS of 90 days, with a recurrence rate of approximately 50% at 100 days post randomization. Because the disease progressed aggressively, most of the subjects did not have adequate drug exposure prior to tumor recurrence. The placebo group (n=75) with no tumor invasion has a median RFS of 236 days, with a recurrence rate of approximately 25% at 100 days post randomization. This demonstrated that there are quite notable differences in the recurrences between subjects with and without tumor invasion.

Subgroup	Median RFS	Relapse rate at 100 days post randomization (approximately)
Placebo with tumor invasion (n=75)	90 days	50%
Placebo with no tumor invasion (n=75)	236 days	25%

2. There are notable differences in drug exposure time between the tumor invasion subgroup and no tumor invasion subgroup.

Because the subjects with tumor invasion were in serious condition, the drug effects might not have had a chance to kick in before tumor relapse occurred. And a vast majority of subjects stopped the study medication after relapse occurred. In this subgroup, the proportion of subjects used 3 cycles or less was 51.7% (77/149), with a median drug exposure of 3 treatment cycles. Due to the short average drug exposure, the drug effect might be minimal.

On the other hand, subjects with no tumor invasion were in relatively better condition. In this subgroup, the proportion of subjects used 3 cycles or less was 24.8% (37/149), with a median drug exposure of 6 treatment cycles, twice as that of subgroup with tumor invasion. Due to the longer average drug exposure time, there is a better chance for drug effect to kick in. In this subgroup, the relapse rate was notably reduced in the treatment group compared to the placebo group (p=0.37, Figure 3.1). The improvement in OS in the treatment group is more notable (p=0.08, Figure 3.2).

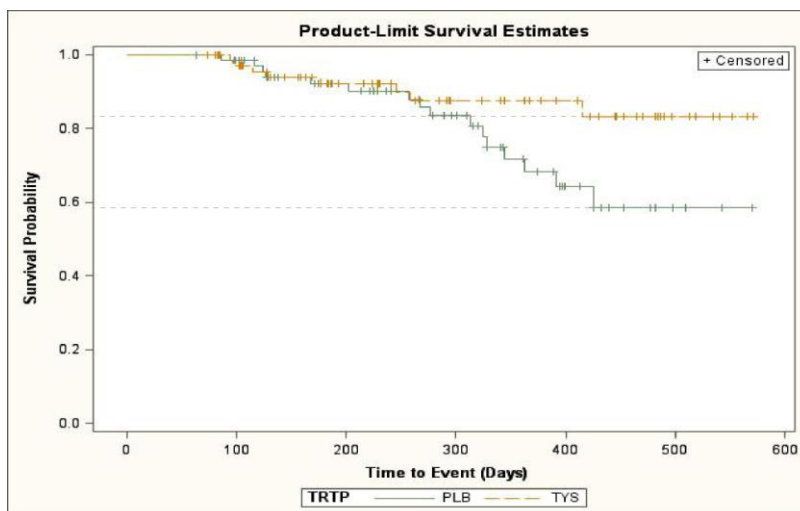
Subgroup	Used $\leq 3$ treatment cycles	Median treatment cycles
With tumor invasion (n=149)	51.7%	3
With no tumor invasion (n=149)	24.8%	6

3. Tumor invasion seriously interfered the primary efficacy evaluation.

The subgroup with tumor invasion was generally in more serious conditions, had faster recurrence, shorter drug exposure time, probably resulting in minimal efficacy. In addition, this subgroup makes up 50% of the overall study population, greatly affects the primary efficacy evaluation. It is believed that this factor could be the main reason why the primary efficacy analysis does not reach statistical significance.

4. Subgroup with no tumor invasion demonstrated favorable trends for treatment effect.

Subjects with no tumor invasion (n=149) were generally in better conditions, had slower recurrence, and longer drug exposure time. Compared to the placebo group, the treatment group had notable favorable trends in both RFS and OS. The favorable trends in OS are more notable (p=0.08). Please see the figure below:



Combined with observations from previous clinical trials, the Group considers that, CMS024 Clinical Trial results clearly indicate that further investigations focusing on the patient populations with milder conditions (such as, subjects with no tumor invasion) with OS as the primary efficacy parameter is highly recommended.

### III. The Group's Next Arrangements for CMS024 Clinical Trial

The Group immediately discussed the preliminary results of CMS024 Clinical Trial with Kangzhe Pharmaceutical Research and Development (Shenzhen) Limited ("Kangzhe R&D"). The Group believes that the CMS024 Clinical Trial clearly indicated the direction of further development of CMS024. The Group's next steps for CMS024 are listed as follows:

1. The CMS024 Clinical Trial results show that OS in the subgroup with no tumor invasion is marginally not significant ( $p=0.08$ , Figure 3.2), and the difference in survival rates at 600 days post randomization exceeds 20%. Because OS is considered as the golden standard for tumor treatment efficacy evaluation, the improvement in OS is critically important. The Group considers it is its responsibility to timely communicate these findings with the China Food and Drug Administration (CFDA).
2. Focusing on the subgroup with no tumor invasion, follow-up data on patient survival will be collected, and updated reports on survival analysis will be submitted to the CFDA in time. These follow-up data on patient survival will also provide clear guidance for further clinical trial design.
3. The Group and Kangzhe R&D intend to carry forward the next steps of the further development of CMS024. Kangzhe R&D will continue to financially sponsor the clinical trials. Meanwhile, the Group also immediately discussed the data trends with the clinicians and statisticians. All of them agreed to continue the collaboration with the Group on the next steps of the clinical trial. The Group will further discuss with clinicians and statisticians the data from CMS024 Clinical Trial and arrangements for the next steps of clinical development. Accordingly, protocol design for the next stage of CMS024 clinical development will be proposed. The Group expects to kick off next CMS024 Clinical Trial by year end.

#### **IV. Risk Warnings**

1. The Group plans to discuss with the CFDA on the results of CMS024 Clinical Trial and the following clinical trial design. In the case that the CFDA does not support the Group to carry out further CMS024 clinical trials, the Group will adhere to the decision of the CFDA.
2. Information disclosed in this announcement is only the preliminary analysis results of CMS024 Clinical Trial. Relevant departments of statistical analysis also need to perform final verifications on all statistical analyses strictly following standard procedures. In an event that negative information surfaces regarding the continued development of the clinical trial, the Group may terminate further clinical development.
3. The Group does not exclude the possibility that the study design of the further clinical trial fails to pass the review of Ethics Committee of clinical institutions resulting in the termination of the clinical study.

The Company will continue to pay close attention to the relevant progress of CMS024 Clinical Trial and fulfill the obligation of disclosure in a timely manner.

By Order of the Board  
China Medical System Holdings Limited  
**Lam Kong**  
*Chairman*

5 March 2014, Hong Kong

*As at the date of the announcement, the directors of the company include (i) executive directors: Mr. Lam Kong, Mr. Chen Hongbing, Ms. Chen Yanling, Mr. Hui Ki Fat and Ms. Sa Manlin; (ii) Independent non-executive directors: Mr. Cheung Kam Shing, Terry, Mr. Huang Ming and Mr. Wu Chi Keung.*