China Healthcare Sector

The race for a COVID-19 vaccine

- **Vaccines could be the final solution for COVID-19 pandemic.** As of 16 May, cumulative COVID-19 cases surpassed 4.6mn in overseas countries while cumulative mortality rate has slightly declined to 6.7% over the past week. The outbreak in major developed countries in western Europe and North America have been gradually controlled. However, many developing countries are at early stage of the outbreak. We highlight that Brazil, Russia and India recorded surging infected cases and may become the next center of coronavirus pandemic.
- **Outbreak to last longer than expected**. Worryingly, for overseas countries that have passed the peak of the outbreak, new cases have been declining at a very slow speed. This implies that the outbreak will last longer than we have expected. It has been consensual that the virus will be with human for quite a long time. Hence, vaccines may be final solution to tackle the outbreak. Although several vaccines have started clinical trials in China and overseas, we may still need to wait for approximately at least six months for vaccines to become available for emergency use. According to WHO, there were at least 118 potential COVID-19 vaccines in the works around the world but only eight were in clinical trials. Only two vaccine candidates have entered into phase 2 trials, both were developed by Chinese companies, including Ad5-nCov developed by CanSino (6185 HK, NR) and another candidate developed by CNBG.
- **Limited data have been revealed on COVID-19 vaccine candidates.** On 18 May (EST), Moderna (MRNA US, NR) released Phase I interim data for its COVID-19 vaccine candidate, mRNA-1273. Based on the released data, all vaccinated subjects had immune response, and eight subjects have developed neutralizing antibodies. In addition, two other COVID-19 vaccine candidates also published preclinical animal data recently, including ChAdOx1 nCoV-19 from The Jenner Institute in the University of Oxford and PiCoVacc from Sinovac Biotech (SVA US, NR) based in China. Both ChAdOx1 nCoV-19 and PiCoVacc showed immunogenicity in rhesus macaques (恒河猴).

- **Major types of COVID-19 vaccine**. There are majorly five types of COVID-19 vaccines by classification of development technologies, including inactivated vaccine, recombinant protein vaccine, viral vector-based vaccine, RNA vaccine, and DNA vaccine (See Figure 1). Moderna's mRNA-1273 is an RNA vaccine. Cansino's Ad5-nCov and Oxford's ChAdOx1 nCoV-19 are viral vector-based vaccine while Sinovac's PiCoVacc is an inactivated vaccine.

- **Development of vaccines against COVID-19 is still in an early stage** at this point and limited data were disclosed. Some vaccine candidates in overseas countries were pushed into clinical phase even without supportive animal data. However, we think some leading candidates might benefit from significant first mover advantage in the future, including Ad5-nCov from Cansino (6185 HK, NR).

MARKET PERFORM (Maintain)

China Healthcare Sector

Jill WU, CFA
(852) 3900 0842
jillwu@cmbi.com.hk

Sam Hu, PhD
(852) 3761 0882
samhu@cmbi.com.hk

Amy Ge
(852) 3761 8778
amyge@cmbi.com.hk

Related Reports

1. Release of NRDL negotiation results; overhang removed for domestic PD-1 drugs – 29 Nov 2019
2. Worse-than-expected price cut; eye on R&D names – 25 Sep 2019
3. Sector intact on government initiated audit – 6 Jun 2019
4. Policy relaxed; eye on innovations and non-medicine sector – 2 Feb 2019
5. Policies favor leading players; Pay attention to oversold stock. – 19 Jul 2018

Overview of recent vaccine data:

For mRNA-1273, Moderna revealed very limited information of the Phase I trial while the safety and efficacy (immunogenicity and neutralizing antibody) data remains to be monitored for a longer period. Moderna stated that all 45 subjects in Phase I (25mg/100mg/250mg cohorts) have developed binding antibodies, but only noticed eight subjects in 25mg and 100mg cohorts have developed neutralizing antibodies. We don't know whether the remaining 37 subjects would develop neutralizing antibodies or not. Moderna stated the levels of binding antibodies in 25mg and 100mg cohorts were similar to or greater than the level of the convalescents. However, how long the binding antibodies level could last remains a question mark. In addition, Moderna didn't disclose the exact concentration of binding antibodies in vaccinated subjects, given that the binding antibodies levels in convalescents could vary a lot. There is no doubt that mRNA-1273 is the most concerned RNA vaccine candidate. However, this technique is new for vaccine development. Given the limited data released by Moderna, it might be too early to judge the outlook of mRNA-1273 before complete safety and efficacy data are available.

For PiCoVacc, Sinovac published a paper in *Science* on 6 May, indicating PiCoVacc could induce neutralizing antibodies in mice, rats and rhesus macaques. Two different doses of PiCoVacc (3μg and 6μg) could provide partial or complete protection in rhesus macaques against SARS-CoV-2 challenge (See Figure 2). In this study, rhesus macaques were vaccinated three times before virus challenge. Viral loads decreased significantly in all vaccinated macaques and all four macaques that received the high dose (6μg) had no detectable viral loads in pharynx, crissum and lung at day 7 after infection. In the 3μg dose group, viral blip could be partially detected. Although no antibody-dependent enhancement (ADE) was observed in for the vaccinated macaques, further studies need to be carried out with a longer monitoring to assess whether there is manifestation of ADE after antibody titers wane.

For ChAdOx1 nCoV-19, Oxford released a preprint version of a submitted paper stating that ChAdOx1 nCoV-19 worked to protect rhesus macaques. Six macaques that received the ChAdOx1 nCoV-19 vaccine 28 days before being infected with SARS-CoV-2 were compared with three control macaques that did not receive the vaccine. The vaccinated animals showed no signs of virus replication in the lungs, significantly lower levels of respiratory disease and no lung damage compared to control animals. The most controversial data were that ChAdOx1 nCoV-19 showed no difference in the amount of viral RNA (both gRNA and sgRNA) detected from nasal secretions in the vaccinated monkeys as compared to the unvaccinated animals when exposed to SARS-CoV-2. Furthermore, although the lung viral load in vaccinated animals was prominently lower than unvaccinated ones, the genomic RNA (gRNA) in lung tissue was not low enough (dozens of gRNA/g were detected). However, this is preliminary and pre-clinical result of ChAdOx1 nCoV-19. Someone compare this result with PiCoVacc's pre-clinical study which we think is somehow unfair: in the PiCoVacc study, macaques were vaccinated three times before exposed to SARS-CoV-2, but in ChAdOx1 nCoV-19 study, macaques were only vaccinated one time. And it might take longer time for ChAdOx1 nCoV-19 to eliminate viral RNA than an inactivated vaccine.

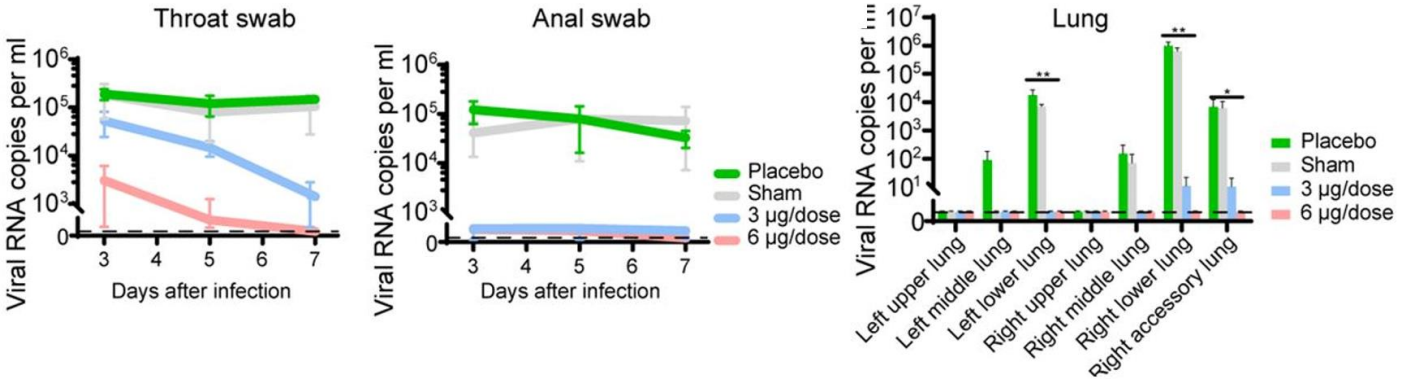
To summarize, the mRNA-1273 might be safe at 25mg and 100mg doses, but needs more data to prove its efficacy. PiCoVacc showed outstanding protection from SARS-CoV-2 inflection in animal studies, especially for 6μg group, but more studies will be necessary to confirm if there is any risk of ADE. Single dose of ChAdOx1 nCoV-19 can provide partial protection from SARS-CoV-2 in macaques while the protection may not be enough. Dose and frequency of ChAdOx1 nCoV-19 vaccination might need to be optimized, in our view.

Figure 1: Major progress of COVID-19 vaccine candidates in China and ex-China

Vaccine classification	Company/Institute	Candidate	Pre-Clinical	Phase I	Phase II	Phase III	Expected milestones
Inactivated Vaccine	国药集团中国生物武汉所			Phase I/II started 12-Apr	PhII stage Started 24-Apr		
	科兴生物/中国医学科学院/浙江疾控	**PiCoVacc**		Phase I/II started 17-Apr	Plan to start in May/June	Plan to start by year end	
Recombinant protein Vaccine	Novavax/Emergent Biosolution	**NVX-coV2373**		Plan to start in May			Preliminary data expect to be available in July. Phase II data expect to be available by year end.
	Sanofi/GSK	**Unnamed**		Plan to start in 2H20			Expect to be granted EUA in 2H21.
	万泰生物/厦门大学/GSK						
	智飞科龙/中科院						
Viral vector-based Vaccine	Vaxart						
	Johnson & Johnson	**Ad26 SARS-CoV-2**		Plan to start in Sep			Preliminary data expect to be available in Dec. Expect to be granted EUA in 1Q21.
	University of Oxford/Vaccitech	**ChAdOx1 nCoV-19**		Started 23-Apr		Plan to start this fall	Expect to be granted EUA in Sep.
	华兰生物/香港大学/厦门大学						
	康希诺/军事医学科学院	**Ad5-nCov**		Started Mid-Mar	Started 12-Apr		Preliminary data expect to be available in May.
RNA Vaccine	珠海丽凡达						
	浙江特瑞斯/四川大学						
	冠昊生物						
	斯微生物						
	BioNTech/Pfizer	**BNT162**		Phase I/II started late Apr			Expect to be granted EUA in Oct.
	CureVac						
	Moderna/NIH	**mRNA-1273**		Started 16-Mar	plan to start in 2Q20	plan to start in Jul 2020	Phase I interim data published on 18-May. Preliminary data expect to be available in 2Q20. Expect to be granted EUA this fall.
DNA Vaccine	北京民海						
	Inovio/艾尔维欣/康泰生物	**INO-4800**		Started 6-Apr	Phase II/III plan to start this summer		Preliminary data expect to be available in end-Jun.

Source: Company website; Note: EUA=Emergency Use Authorization

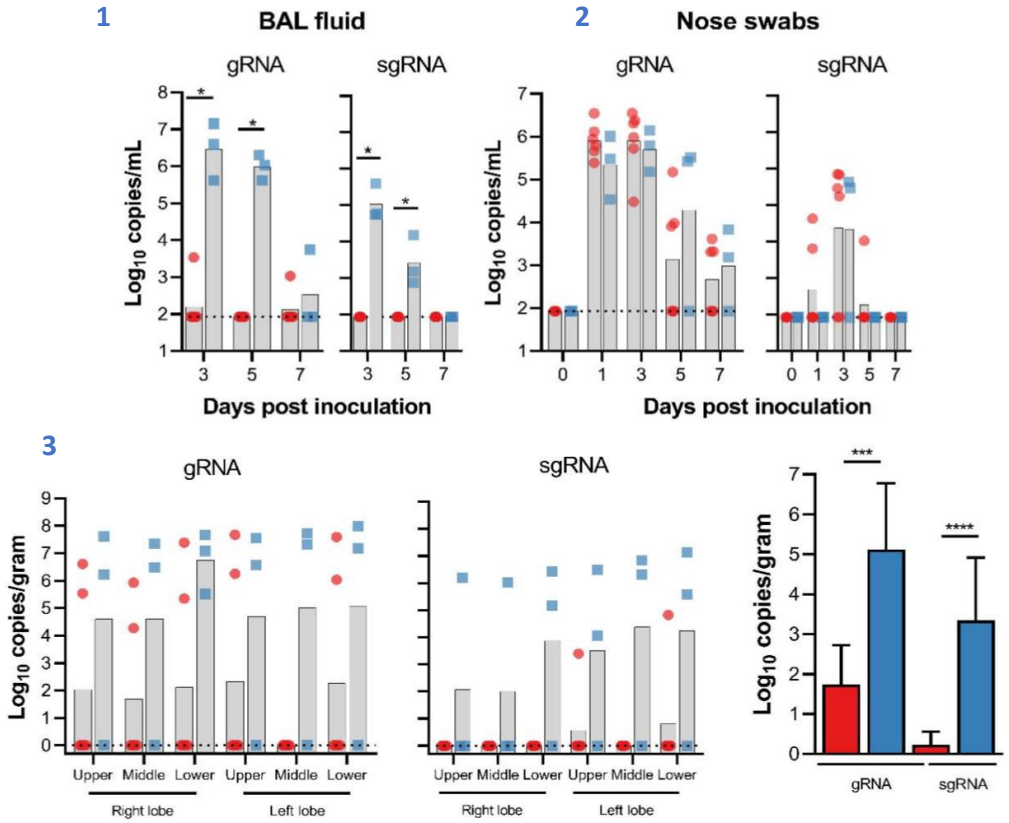
Figure 2: Viral loads of throat and anal swab specimens collected from the inoculated macaques



Note: Viral loads of throat and anal swab specimens collected from the inoculated macaques at day 3, 5 and 7 post-infection were monitored. Viral loads in various lobes of lung tissue from all the inoculated macaques at day 7 post-infection were measured.

Source: Q. Gao et al., Science. 10.1126/science.abc1932 (2020).

Figure 3: Clinical signs and viral load in rhesus macaques inoculated with SARS-CoV-2 after vaccination with ChAdOx1 nCoV-19



Note: 1. Viral load in BAL fluid obtained from rhesus macaques, bar at geometric mean. 2. Viral load in nose swabs obtained from rhesus macaques, bar at geometric mean. 3. Viral load in tissues at 7 days post inoculation. Pictured are individual values with geometric mean bars (left panels) and geometric mean of all lung lobes per group (right panel).

Source: N van Doremalen et al. bioRxiv 2020.05.13.093195; doi: https://doi.org/10.1101/2020.05.13.093195

Disclosures & Disclaimers

Analyst Certification

The research analyst who is primary responsible for the content of this research report, in whole or in part, certifies that with respect to the securities or issuer that the analyst covered in this report: (1) all of the views expressed accurately reflect his or her personal views about the subject securities or issuer; and (2) no part of his or her compensation was, is, or will be, directly or indirectly, related to the specific views expressed by that analyst in this report.

Besides, the analyst confirms that neither the analyst nor his/her associates (as defined in the code of conduct issued by The Hong Kong Securities and Futures Commission) (1) have dealt in or traded in the stock(s) covered in this research report within 30 calendar days prior to the date of issue of this report; (2) will deal in or trade in the stock(s) covered in this research report 3 business days after the date of issue of this report; (3) serve as an officer of any of the Hong Kong listed companies covered in this report; and (4) have any financial interests in the Hong Kong listed companies covered in this report.

CMBIS Ratings

BUY	: Stock with potential return of over 15% over next 12 months
HOLD	: Stock with potential return of +15% to -10% over next 12 months
SELL	: Stock with potential loss of over 10% over next 12 months
NOT RATED	: Stock is not rated by CMBIS
OUTPERFORM	: Industry expected to outperform the relevant broad market benchmark over next 12 months
MARKET-PERFORM	: Industry expected to perform in-line with the relevant broad market benchmark over next 12 months
UNDERPERFORM	: Industry expected to underperform the relevant broad market benchmark over next 12 months

CMB International Securities Limited

Address: 45/F, Champion Tower, 3 Garden Road, Hong Kong, Tel: (852) 3900 0888 Fax: (852) 3900 0800

CMB International Securities Limited ("CMBIS") is a wholly owned subsidiary of CMB International Capital Corporation Limited (a wholly owned subsidiary of China Merchants Bank)

Important Disclosures

There are risks involved in transacting in any securities. The information contained in this report may not be suitable for the purposes of all investors. CMBIS does not provide individually tailored investment advice. This report has been prepared without regard to the individual investment objectives, financial position or special requirements. Past performance has no indication of future performance, and actual events may differ materially from that which is contained in the report. The value of, and returns from, any investments are uncertain and are not guaranteed and may fluctuate as a result of their dependence on the performance of underlying assets or other variable market factors. CMBIS recommends that investors should independently evaluate particular investments and strategies, and encourages investors to consult with a professional financial advisor in order to make their own investment decisions.

This report or any information contained herein, have been prepared by the CMBIS, solely for the purpose of supplying information to the clients of CMBIS or its affiliate(s) to whom it is distributed. This report is not and should not be construed as an offer or solicitation to buy or sell any security or any interest in securities or enter into any transaction. Neither CMBIS nor any of its affiliates, shareholders, agents, consultants, directors, officers or employees shall be liable for any loss, damage or expense whatsoever, whether direct or consequential, incurred in relying on the information contained in this report. Anyone making use of the information contained in this report does so entirely at their own risk.

The information and contents contained in this report are based on the analyses and interpretations of information believed to be publicly available and reliable. CMBIS has exerted every effort in its capacity to ensure, but not to guarantee, their accuracy, completeness, timeliness or correctness. CMBIS provides the information, advices and forecasts on an "AS IS" basis. The information and contents are subject to change without notice. CMBIS may issue other publications having information and/ or conclusions different from this report. These publications reflect different assumption, point-of-view and analytical methods when compiling. CMBIS may make investment decisions or take proprietary positions that are inconsistent with the recommendations or views in this report.

CMBIS may have a position, make markets or act as principal or engage in transactions in securities of companies referred to in this report for itself and/or on behalf of its clients from time to time. Investors should assume that CMBIS does or seeks to have investment banking or other business relationships with the companies in this report. As a result, recipients should be aware that CMBIS may have a conflict of interest that could affect the objectivity of this report and CMBIS will not assume any responsibility in respect thereof. This report is for the use of intended recipients only and this publication, may not be reproduced, reprinted, sold, redistributed or published in whole or in part for any purpose without prior written consent of CMBIS.

Additional information on recommended securities is available upon request.

For recipients of this document in the United Kingdom

This report has been provided only to persons (I)falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended from time to time)("The Order") or (II) are persons falling within Article 49(2) (a) to (d) ("High Net Worth Companies, Unincorporated Associations, etc.,) of the Order, and may not be provided to any other person without the prior written consent of CMBIS.

For recipients of this document in the United States

This report is intended for distribution in the United States to "major US institutional investors", as defined in Rule 15a-6 under the US, Securities Exchange Act of 1934, and may not be furnished to any other person in the United States. Each major US institutional investor that receives a copy of this research report by its acceptance hereof represents and agrees that it shall not distribute or provide this research report to any other person.

For recipients of this document in Singapore

This report is distributed in Singapore by CMBI (Singapore) Pte. Limited (CMBISG) (Company Regn. No. 201731928D), an Exempt Financial Adviser as defined in the Financial Advisers Act (Cap. 110) of Singapore and regulated by the Monetary Authority of Singapore. CMBISG may distribute reports produced by its respective foreign entities, affiliates or other foreign research houses pursuant to an arrangement under Regulation 32C of the Financial Advisers Regulations. Where the report is distributed in Singapore to a person who is not an Accredited Investor, Expert Investor or an Institutional Investor, as defined in the Securities and Futures Act (Cap. 289) of Singapore, CMBISG accepts legal responsibility for the contents of the report to such persons only to the extent required by law. Singapore recipients should contact CMBISG at +65 6350 4400 for matters arising from, or in connection with the report.