World's First Candidate Antibody Treatment for Yellow Fever, Developed by Tychan, Tested Safe and Effective in Human Volunteers

- Phase 1A/1B safety and efficacy trials in Singapore completed within 8 months
- TY014 also found to prevent vaccine related adverse effects in vaccinated volunteers

Singapore –14 NOVEMBER, 2019 – Tychan's first-in-class monoclonal antibody candidate treatment for Yellow Fever (YF), called TY014, has successfully completed Phase 1A/1B safety trials in Singapore, it announced today. Tychan received regulatory approval from the Health Sciences Authority (HSA) of Singapore in November last year to conduct human trials for TY014, after a record setting timeline of 7 months from candidate to regulatory submission. Tychan has also received regulatory approval in Brazil to conduct a field study in YF affected areas.

Using a novel clinical design, the trials were initially conducted in healthy volunteers before also being tested in volunteers vaccinated with yellow fever vaccine. The results indicated that TY014 was not only safe and well tolerated at the highest doses tested, but also suppressed vaccine virus and related adverse effects. The safety, efficacy and pharmacokinetic data will be presented at the Late-Breaker session of this year's annual conference of the American Society of Tropical Medicine and Hygiene (ASTMH) held November 20th– November 24th at the Gaylord National Resort and Convention Center National Harbor, Maryland USA.

YF is a mosquito-borne haemorrhagic disease caused by the Yellow Fever Virus (YFV) endemic to 47 countries in Sub-Saharan Africa, Central and South America for which there are no treatment options available. According to the Centre for Disease Control (CDC) in Atlanta, USA, nearly 15% of the patients infected with YFV develop life threatening illness involving haemorrhage, jaundice, and shock, often leading to death. Despite the existence of an effective YFV vaccine, a sudden spurt in global demand from ongoing outbreaks has resulted in a shortage that leaves millions at risk, especially in Africa and South America. In Brazil alone, 723 cases with 237 deaths were reported between July 2017 and February 2018 and additional outbreaks in Ethiopia where 10 deaths were reported. Although the seasonal outbreak in the summer of 2018 in Brazil was substantially less, Yellow Fever outbreaks have continued in Africa and there remains a critical unmet medical need for a therapeutic option for this deadly disease. Moreover, those who receive vaccination, especially the vulnerable or high risk groups, remain at risk of serious and life threatening vaccine-related adverse effects with no treatment options.

"This is an exciting development towards a strategy for intervention in YF disease for which no treatment exists, and I look forward to field studies which will provide additional scientific rationale for TY014," said *Dr Mauro Teixeira, Professor of Immunology at the Department of Biochemistry and Immunology, Universidade Federal de Minas Gerais, Brazil, and principal investigator of the field study for TY014 in Brazil*.

"The successful trial paves the way for a first of its kind treatment for yellow fever. This rapid development following the similar achievement for Zika affirms the first ever innovative technology platform and boosts the confidence in Tychan's development of rapid response capability against deadly infectious diseases. It brings us one step closer to our ultimate objective of addressing sudden infectious disease outbreaks," said Teo Ming Kian, Chairman of the Board, Tychan.

Rapid development and manufacture of TY014 and Tyzivumab – the Zika therapeutic, were both completed in record times enabled by a joint partnership with WuXi Biologics. The completion of Phase 1 trials for both of its infectious disease pipeline products occurred within 8 months of IND approval.

"Congratulations to Tychan on reaching another great milestone with the world's first Yellow Fever antibody candidate. We are proud to empower Tychan's achievements through our single-source integrated biologics

technology platform, expediting the timeline of biologics from DNA to clinical trials. Leveraging our strong expertise and capabilities to accelerate the development and manufacture of innovative biologics, WuXi Biologics continues to empower global partners, allowing them to provide more life-saving treatments to meet emerging health challenges," said Chris Chen, CEO WuXi Biologics.

Tychan's technology platform was developed by its founders, Professor Ram Sasisekharan of Massachusetts Institute of Technology (MIT) /Singapore MIT Alliance for Research and Technology (SMART) and Professor Ooi Eng Eong, Deputy Director, Emerging Infectious Diseases Programme, Duke-NUS Medical School, Singapore and Co-Director, Viral Research and Experimental Medicine Centre@SingHealth Duke-NUS (ViREMiCS) with funding support from Temasek Holdings, Singapore.

The rapid regulatory approval by HSA of TY014 as well as Tyzivumab, the world's first Zika therapeutic candidate, coupled with speedy completion of safety trials is a validation of Tychan's innovations in development and production cycles for manufacturing as well as regulatory acceptance. Tychan aims to further its development platform and build on such partnerships to accelerate timely delivery of safe and effective therapeutics that are critical for preparedness against pandemics caused by additional emerging infectious agents like YFV and Zika for which no treatment options exist.

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For media reference:

About TY014

TY014 is the first monoclonal antibody designed and engineered to treat Yellow Fever Virus infected patients to enter the clinic. TY014 is directed against the envelope (E) protein on the surface of the virus, and prevents viral replication by limiting viral fusion to host cells.

About the Trial

The first in human clinical trial was conducted in Singapore in approximately 27 healthy volunteers. Volunteers in the Phase 1 trial were split into 2 parts and randomised into one of five dose cohorts, each receiving a single dose of TY014 or placebo. The primary endpoints of the study were safety and tolerability and secondary endpoints include pharmacokinetics and immunogenicity. In the second part the volunteers received live attenuated yellow fever vaccine before treatment with TY014 or placebo. The primary end pints of this arm was safety and tolerability as well as complete aviremia in treatment cohorts. The trial was administered by SingHealth Investigational Medicine Unit, led by Associate Professor Jenny Low, Senior Consultant, Department of Infectious Diseases, Singapore General Hospital and Co-Director, Viral Research and Experimental Medicine Centre@SingHealth Duke-NUS (ViREMiCS).

About Yellow Fever Virus

Yellow Fever Virus (YFV) is a single-stranded RNA virus in the genus Flavivirus, thus phylogenetically related to Dengue, West Nile, Zika and Japanese encephalitis viruses. Yellow Fever (YF) is an acute viral haemorrhagic disease caused by the Yellow Fever Virus (YFV), a re-emerging arbovirus transmitted by the same mosquito vector (*Aedes aegypti*) that transmits Dengue virus (DENV) and Zika virus (ZIKV). Clinical symptoms of YF include fever, chills, headaches, jaundice, muscle aches, nausea and fatigue, with ~15% of YFV-infected patients going on to develop life-threatening complications of haemorrhage, jaundice and shock, which often lead to death. YFV is endemic in tropical and subtropical areas of South America and Africa, causing an estimated 200,000 infections and 30,000 deaths annually. It has now become a growing public health problem, rapidly spreading throughout the two (2) continents in a cyclical pattern. The current outbreak in Brazil has sparked great concerns that it would potentially become a full-blown urban epidemic with 300 deaths already recorded since the outbreak started in July 2017. To date, there have been at least 10 international travellers who have contracted the disease with four (4) reported deaths. With climate change, global travel and urbanisation, which increase the chance for mosquito-borne diseases to spread rapidly, the risk of YFV establishing its foothold in the Asia-Pacific region with periodic epidemic bursts remains a real public health concern. Although there is currently a safe and effective vaccine available on the market, global shortages of supplies have severely hampered any efforts in the prevention and control of YFV outbreaks. To date, no YFV therapy (biologic or small molecule) has advanced to clinical trials. It is anticipated that a monoclonal antibody therapeutic could be administered to infected cases to reduce disease severity within the patient and their contacts.

About Tychan

Tychan, a Singapore clinical-stage biotechnology company, is focused on bringing life-saving treatments for emerging infections to those in need through disruptive technologies. In a coordinated effort with regulatory authorities, we are accelerating the translation from non-clinical studies to clinical trials for emerging pathogens. Founded by Professor Ram Sasisekharan of Massachusetts Institute of Technology (MIT) /Singapore MIT Alliance for Research and Technology (SMART) and Professor Ooi Eng Eong of Duke- National University of Singapore (Duke-NUS), their expertise spans the fields of biologics development and biology of acute viral infections. Temasek Holdings is the founding investor of Tychan Pte. Ltd. For more information on Tychan Pte Ltd, please visit: www.tychan.com

About WuXi Biologics

WuXi Biologics (stock code: 2269.HK), a Hong Kong-listed company, is a leading global open-access biologics technology platform offering end-to-end solutions to empower organizations to discover, develop and manufacture biologics from concept to commercial manufacturing. Our company history and achievements demonstrate our commitment to providing a truly ONE-stop service offering and strong value proposition to our global clients. As of June 30, 2019, there were a total of 224 integrated projects, including 106 projects in pre-clinical development stage, 102 projects in early-phase (phase I and II) clinical development, 15 projects in late-phase (phase III) development and 1 project in commercial manufacturing. With total estimated capacity for biopharmaceutical production planned in China, Ireland, Singapore and US exceeding 280,000 liters by 2022, we will provide our biomanufacturing partners with a robust and premier-quality global supply chain network. For more information on WuXi Biologics, please visit www.wuxibiologics.com.

About Temasek

Incorporated in 1974, Temasek is an investment company headquartered in Singapore. Supported by 11 offices internationally, Temasek owns a S$275 billion portfolio as at 31 March 2017, mainly in Singapore and the rest of Asia. Our portfolio covers a broad spectrum of industries: financial services; telecommunications, media & technology; transportation & industrials; consumer & real estate; life sciences & agribusiness; as well as energy & resources. As an institution, we have a stake in the well-being of our larger community. We recognise that environmental, social and governance factors can impact our stakeholders as well as the long term sustainability of companies and businesses. As an institution, we have a stake in the well-being of our larger community. We recognise that environmental, social and governance factors can impact our stakeholders as well as the long term sustainability of companies and businesses.

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