Annex III K. 6/115 amended

# Development of bismuth drugs for the treatment of microbial infections

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#### **Summary of the Impact**

Prof. Hongzhe Sun's research has made international impact on the development of inorganic pharmaceutics and providing prospective therapeutic options for major diseases.

- He determined the structure of bismuth drugs in gastric fluid and systematically deciphered their anti-*Helicobacter pylori* mode of mechanism, which has been embodied in the textbook and utilized as the principle of bismuth-based antiulcer drugs development in China.
- He firstly proposed bismuth drug as anti-SARS-CoV agent in 2007 and demonstrate their *in vivo* potency against SARS-CoV-2 during COVID-19 pandemic, which provided the base of phase 3 clinical trial on COVID-19 patients treated with oral bismuth in China.
- He initiated the area of bismuth drug as antimicrobial resistance breaker for the treatment of (multi)drug-resistant bacterial infections.

#### **Underpinning Research**

#### ✓ We have >200 publications



✓ >4 patent granted/filed

✓ 1 RIF grants
2 CRF grants
3 ITF grants

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Norman & Cecilia Yip endowed Professorship in Bioinorganic Chemistry



WuXi AppTech Life Science & Chemistry Research Åward (2016)

UC Berkeley Earl L Muetterties Memorial Lectureship (2018)

#### **Outline of underpinning Research**



Deciphering of bismuth drugs in simulated gastric acid and their mode of action against *Helicobacter pylori* 

-Since 2002, project leader



Development of bismuth drug as antiviral agents

 —Since 2003, project leader, cooperator: Prof. Kwok-Yung Yuen, Prof. Jiandong Huang, Prof. Bojian Zheng, Dr. Shuofeng Yuan



Overcoming antimicrobial resistance by bismuth drugs

—Since 2014, project leader cooperator: Dr. Richard Yi-Tshun Kao, Dr. Pak-Leung Ho

#### Structure of bismuth drugs in simulated gastric acid



#### **Bioinorganic approach for COVID-19**

Bismuth drugs are effective against SARS-CoV-2 (therapeutic index > 900)

Bismuth suppresses the replication of the virus in animal model



(Yuan SF, Wang RM, Chan JFW,... Yuen KY, Sun H, Nature Microbiol 2020, 5, 1439)

#### New approach to fight against infection by superbugs: metallodrugs

#### > Bismuth drugs are selectively toxic to microbe based on metalloproteomics studies

Bismuth drug inactivate key resistant determinant NDM-1 in superbugs





Wang RM, Lai ZP,... Li H, Sun H, *Nature Comm.* 2018, *9*, 439 Sun H, Zhang Q, Wang RM, Wang HB... Li HY, *Nature Comm.* 2020, *11*, 5263 Sun, Wang, Li, Kao, Zhang, US patent: 10,201,518 B2

## **Impacts Achieved**

Partial work was selected in the *Inorganic Chemistry* textbook (Armstrong et al, Oxford University Press, 2014)





Weller M., Overton T., Rourke J., Armstrong F. "*Inorganic Chemistry*", Oxford University Press, 2014, p422

Rehder D. "*Bioinorganic Chemistry*", Oxford University Press, 2014, p42

### **Impacts Achieved**

>37k accesses

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providing scientific basis for the phase III/IV clinical trial on COVID-19 patients treated with oral bismuth drugs (ChiCTR2000030398 and NCT04811339)



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