Ascletis Pharma Inc.
歌禮製藥有限公司
(incorporated in the Cayman Islands with limited liability)
(Stock Code: 1672)

INSIDE INFORMATION

BUSINESS UPDATE: 3CLPRO INHIBITOR ASC11 DEMONSTRATED POTENTIAL TO BE EFFECTIVE TREATMENT FOR COVID-19

- *In antiviral cellular assays, antiviral potency (EC_{90}) of ASC11 is 31-fold of that of Nirmatrelvir, 120-fold of that of S-217622, 16-fold of that of PBI-0451 and 7-fold of that of EDP-235.*

- *ASC11 is an in-house discovered oral small molecule drug candidate, targeting 3CLpro, with global intellectual property rights.*

- *It is expected that IND of ASC11 will be filed in the second half of 2022 and Phase I clinical trial in healthy subjects will be completed by the end of 2022.*

This announcement is made by Ascletis Pharma Inc. (the "**Company**" or "**Ascletis**") pursuant to Rule 13.09(2)(a) of the Rules (the "**Listing Rules**") Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited (the "**Stock Exchange**") and the Inside Information Provisions under Part XIVA of the Securities and Futures Ordinance (Chapter 571 of the Laws of Hong Kong).

The board (the "**Board**") of directors (the "**Directors**") of the Company announces that its oral small molecule drug candidate ASC11, a 3-chymotrypsin like protease (3CLpro) inhibitor, demonstrated potential to be effective treatment for COVID-19.

In antiviral cellular assays with infectious SARS-CoV-2, antiviral potency (EC_{90}) of ASC11 is 31-fold (155/5) of that of Nirmatrelvir; 120-fold (600/5) of that of S-217622; 16-fold (78/5) of that of PBI-0451 and 7-fold (33/5) of that of EDP-235 (Table 1). Importantly, ASC11 activity was retained against different SARS-CoV-2 variants.

Table 1. Antiviral Potency (EC_{90}) of ASC11 versus Global Leading 3CLpro Inhibitors

3CLpro inhibitor	ASC11[2]	Nirmatrelvir[3]	S-217622[4]	PBI-0451[5]	EDP-235[6]
Vero E6 Cell EC_{90}[1] (nM)	5	155	600	78	33

Notes:

1. EC_{90}: a measure of drug potency showing a concentration that is effective in producing 90% of the maximal virus reduction. Lower the numbers, greater the antiviral potency. Compared to EC_{50} (a concentration that is effective in producing 50% of the maximal virus reduction), EC_{90} can predict more precisely the effective concentration of an antiviral drug in humans.

2. Data from the antiviral cellular assay with infectious SARS-CoV-2 conducted at IIT Research Institute, headquartered at Illinois Institute of Technology in Chicago, Illinois, U.S.

3. Data from Owen et al., Pfizer Worldwide Research, medRxiv, July 2021, https://doi.org/10.1101/2021.07.28.21261232.

4. EC_{90} estimated from Unoh et al., Shionogi Pharmaceutical Research Center, bioRxiv, January 2022. https://doi.org/10.1101/2022.01.26.477782.

5. Data from the presentation by Pardes Biosciences, Inc. at International Conference on Antiviral Research 2022 (ICAR 2022).

6. Data from the antiviral assay with primary human airway epithelial cells, press release October 19, 2021 by Enanta Pharmaceuticals, Inc.

ASC11 is an in-house discovered oral small molecule drug candidate using various proprietary technologies including molecular docking. ASC11 has global intellectual property rights.

Molecular docking showed that compared to Nirmatrelvir, ASC11 formed stronger hydrogen bond interaction with Glutamic acid 166 of 3CLpro, created new hydrogen bonds with other key amino acids of 3CLpro and fitted more tightly in hydrophobic Pocket 4 (P4) of 3CLpro, resulting in much higher antiviral potency (EC_{90}) of ASC11.

Molecular docking showed ASC11 bound to 3CLpro differently from S-217622, resulting in much higher antiviral potency (EC_{90}) of ASC11.

In Vero E6 cells, safety window (cytotoxicity versus antiviral potency) of ASC11 is more than 10,000-fold.

Together with other preclinical data including Caco-2 permeability, *in vitro* metabolism, microsomal stability and animal pharmacokinetic studies, ASC11 demonstrated potential for best-in-class antiviral treatment of COVID-19.

Ascletis expects that the Investigational New Drug (IND) of ASC11 will be filed in the second half of 2022 and Phase I clinical trial in healthy subjects will be completed by the end of 2022.

The Company's second 3CLpro preclinical candidate (PCC), which is also discovered in-house with global intellectual property rights, demonstrated the same antiviral potency and safety window in Vero E6 cells as compared to ASC11.

Cautionary Statement required by Rule 18A.05 of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited: We cannot guarantee that we will be able to ultimately commercialize ASC11 successfully.

Shareholders and potential investors are advised to exercise caution when dealing in the shares of the Company.

By order of the Board
Ascletis Pharma Inc.
歌禮製藥有限公司
Jinzi Jason WU
Chairman

Hangzhou, the People's Republic of China
April 19, 2022

As at the date of this announcement, the Board comprises Dr. Jinzi Jason WU and Mrs. Judy Hejingdao WU, as executive Directors; and Dr. Yizhen WEI, Mr. Jiong GU and Ms. Lin HUA, as independent non-executive Directors.