

Case No. PGR2025-00057
Patent No. 12,234,236

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CONJUPRO BIOTHERAPEUTICS, INC.,
Petitioner,

v.

ASCLETIS PHARMA CHINA CO. LTD.,
Patent Owner.

Case No. PGR2025-00057
Patent No. 12,234,236
Title: GLP-1R agonist and therapeutic method thereof

**DECLARATION OF JOHN GARGIULO IN SUPPORT OF PATENT
OWNER'S RESPONSE**

I, John Gargiulo, declare as follows:

1. I have personal knowledge of all the facts in this declaration and am competent to testify to them.
2. I joined Ascletis Pharma Inc. in May 2022. Ascletis Pharma Inc. is the parent company of Patent Owner Ascletis Pharma China Co. Ltd. (“Ascletis” or “Patent Owner”), the owner of U.S. Patent No. 12,234,236 (the “’236 Patent”).
3. I am currently the Chief Business Officer of Ascletis Pharma Inc. In this role, I am responsible for Ascletis’ business development functions, expanding the company’s strategic goals internationally. I am also aware and informed of the company’s drug development programs as part of this role. In addition, I often present the results of our preclinical and clinical studies for our drug candidates, including ASC30, to potential investors and strategic partners.
4. I received my Master’s Degree in Business Administration from The Fuqua School of Business at Duke University. And I received a Bachelor of Arts in Economics from Boston College.
5. I submit this declaration to present the results of preclinical studies evaluating the characteristics of certain compounds disclosed and/or claimed in the ’236 Patent and the comparator used in some of those studies, orforglipron.

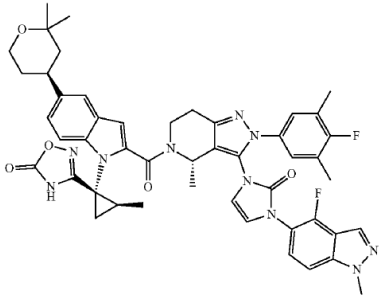
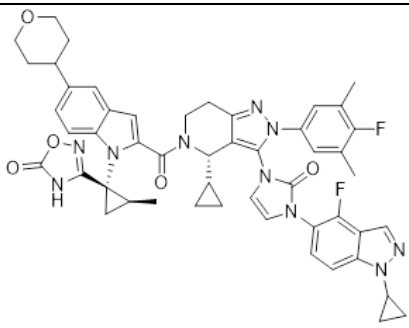
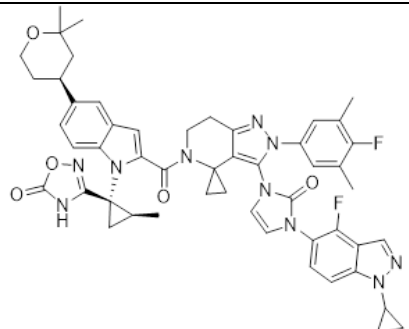
A. Results of In Vitro Activity Evaluation of Claimed Compounds Compared to Orforglipron

6. Ascletis directed the testing of compounds disclosed and/or claimed in the '236 Patent to compare their potency in an hGLP-I R cAMP Assay to orforglipron. The compounds' potency was measured using an hGLP-1R cAMP assay, as described in the Example 2 of the '236 patent ("the hGLP-1R cAMP Assay"). (EX1001, 199:48-201:30.)

7. Table 2 of the '236 Patent discloses the biological activity of certain compounds the hGLP-1R cAMP Assay. The results are expressed as the half maximal effective concentration ("EC₅₀"), which is a measure of potency. (EX1001, 201:1-30, Table 2.) Table 2 of the '236 Patent is reproduced below.

TABLE 2	
Bioactivity of different compounds in hGLP-1R agonist cAMP stimulation assay	
Compounds	hGLP-1R CAMP: EC ₅₀ (nM)
1	0.094
13	0.228
18	0.265
19	0.012
20	0.018
21	0.044
24	0.868
29	0.063
35	0.025
36	0.05
37	0.06
55	0.15
65	0.092
66	0.014
70	0.064
76	0.019
77	0.022
78	0.012
79	0.171
80	0.038
81	0.042
82	0.011
84	0.08
50	0.028

8. In addition to the compounds listed in Table 2 of the '236 Patent, Ascletis evaluated several other compounds using the hGLP-1R cAMP Assay. As can be seen in the chart below, orforglipron had an EC₅₀ value of 0.044 nM in the Activity Study. Two additional compounds not specifically identified in the '236 Patent had EC₅₀ values of 1.995 nM and over 10 nM. The chart below shows the EC₅₀ values observed for these three additional compounds in the hGLP-1R cAMP Assay.

Structure	hGLP-1R agonist cAMP stimulation assay, EC ₅₀ (nM)
 Orforglipron	0.044
	1.995
	>10

B. Results of Single-Dose Subcutaneous Injection in Sprague-Dawley (SD) Rats

9. Ascletis directed the testing of compounds disclosed and/or claimed in the '236 Patent to compare their pharmacokinetics after a single-dose subcutaneous injection. The study was conducted as described in the Example 3 of the '236 patent ("the PK Study"). (EX1001, 201:31-201:67.)

10. Table 3 of the '236 Patent discloses the pharmacokinetics of certain compounds in the PK Study. Table 3 (reproduced below) provides the total drug exposure for 696 hours (AUC_{0-696h}) for Compounds 1, 13, 18, 19, 20, 21 and orforglipron. (EX1001, 202:37-50, Table 4.)

TABLE 3			
Drug exposure of different compounds after a single-dose subcutaneous injection			
Compounds	Dosing route	Dose, mg/kg	AUC_{0-696h} , ng · h/mL
1	Subcutaneous	30	60,272
13	Subcutaneous	30	23,399
18	Subcutaneous	30	51,234
19	Subcutaneous	30	234,473
20	Subcutaneous	30	77,688
21	Subcutaneous	30	61,479
Orforglipron	Subcutaneous	30	5,390

11. In addition to the data listed in Table 3 of the '236 Patent, Ascletis evaluated the clearance (Cl_F) and observed concentration (C_{max}) for Compounds 1

and 19 of the '236 Patent in the PK study. The chart below shows this additional data for Compounds 1 and 19.

	Compound 1	Compound 19
Cl _F , mL/min/kg	7.27	2.03
C _{max} , ng/mL	561	2603

C. Authentication of Laboratory Notebook (EX2081)

12. **Exhibit 2081** is a true and correct copy of Ascletis laboratory notebook GLNB007230-3. Laboratory notebooks, including this laboratory notebook, are maintained in the regular course of business at Ascletis.

13. In Exhibit 2081, GLC02-521 refers to Compound 1 in the '236 Patent and GLC02-568 refers to Compound 65.

I declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made knowing that willful false statements and the like so made are punishable by fine, imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Dated: March 5, 2026

Respectfully submitted,

/s/ John Gargiulo