Supporting Information for

Original article

Discovery of a highly selective VEGFR2 kinase inhibitor CHMFL-VEGFR2-002 as a novel anti-angiogenesis agent

Zongru Jiang[a,b,†], Li Wang[a,b,†], Xuesong Liu[a,b,†], Cheng Chen[a,b,†], Beilei Wang[a,b], Wenliang Wang[a,b], Chen Hu[a], Kailin Yu[a], Ziping Qi[a], Qingwang Liu[c], Aoli Wang[a], Jing Liu[a,d], Guangchen Hong[e,*], Wenchao Wang[a,d,**], Qingsong Liu[a,b,c,d,f,*]**

[a]*High Magnetic Field Laboratory, Key Laboratory of High Magnetic Field and Ion Beam Physical Biology, Hefei Institutes of Physical Science, Chinese Academy of Sciences, Hefei 230031, Anhui, PR China*
[b]*University of Science and Technology of China, Hefei 230026, Anhui, PR China*
[c]*Precision Targeted Therapy Discovery Center, Institute of Technology Innovation, Hefei Institutes of Physical Science, Chinese Academy of Sciences, Hefei 230088, Anhui, PR China*
[d]*Precision Medicine Research Laboratory of Anhui Province, Hefei 230088, Anhui, PR China*
[e]*The People's Hospital of Shinan District, Qingdao 266002, Shandong, PR China*
[f]*Institutes of Physical Science and Information Technology, Anhui University, Hefei 230601, Anhui, PR China*

[*]Corresponding author. Tel.: +86 551 65595161.

E-mail addresses: qsliu97@hmfl.ac.cn (Qingsong Liu), wwcbox@hmfl.ac.cn (Wenchao Wang), 2297023869@qq.com (Guangchen Hong).

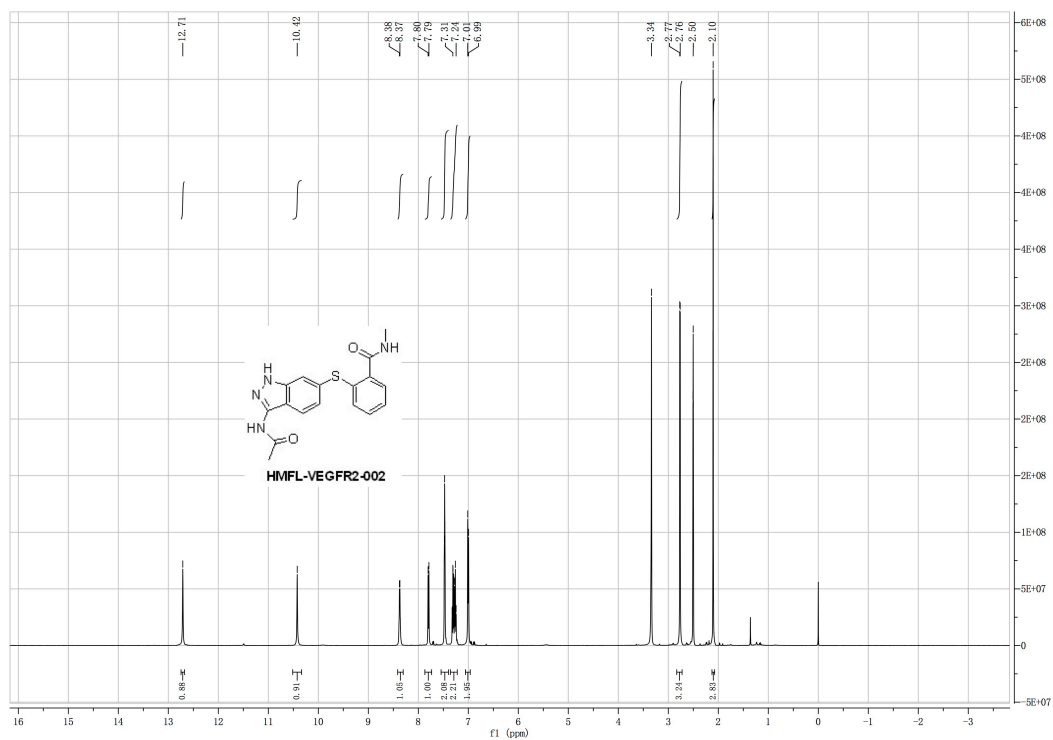[†]These authors made equal contributions to this work.

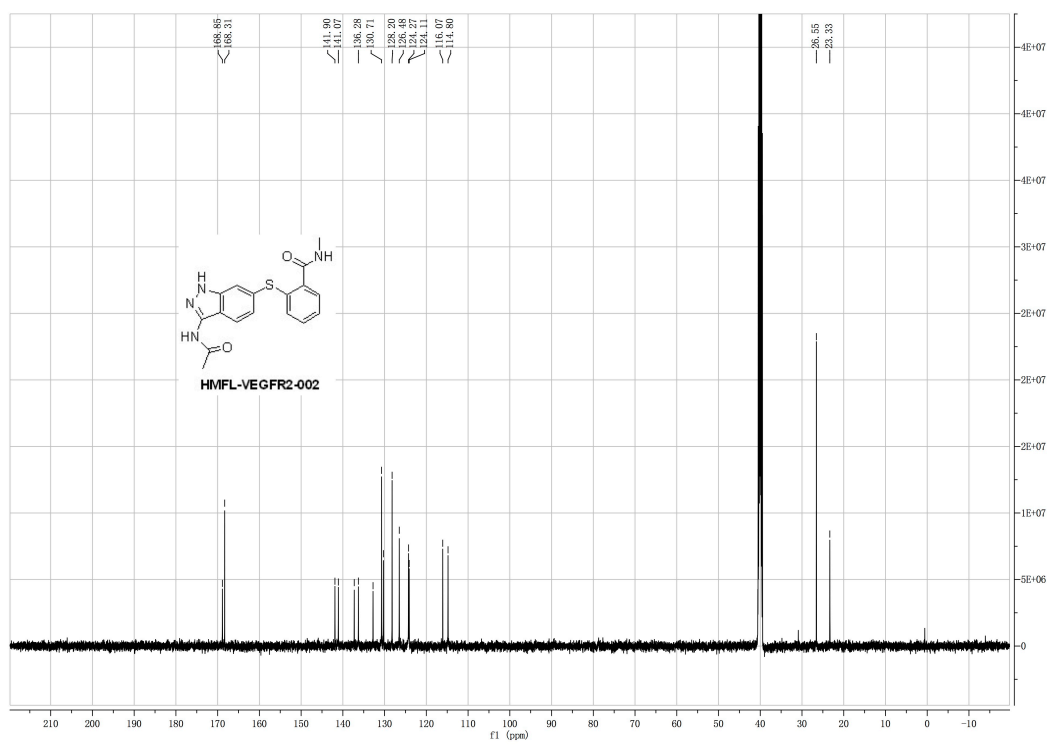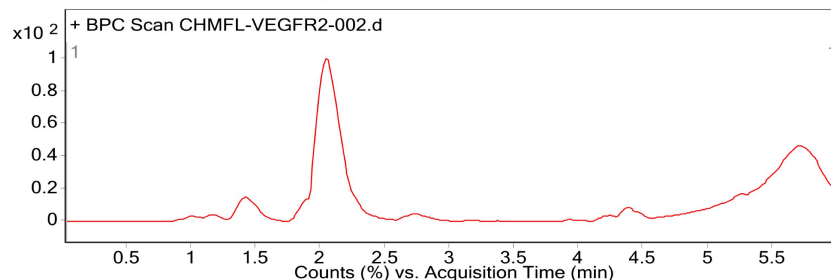**Figure S1** The ^{1}H NMR spectrum of CHMFL-VEGFR2-002.

Figure S2 The ^{13}C NMR spectrum of CHMFL-VEGFR2-002.

Data Filename	CHMFL-VEGFR2-002.d	Sample Name	LXS
Sample Type	Sample	Position	Vial 10
Instrument Name	Instrument 1	User Name	
Acq Method	01012018NORMAL.m	Acquired Time	5/8/2019 11:52:42 AM
IRM Calibration Status	Success	DA Method	3.m
Comment			

Sample Group		Info.	
Acquisition SW	6200 series TOF/6500 series		
Version	Q-TOF B.05.00 (B5042.2)		

User Chromatograms

Fragmentor Voltage 175 **Collision Energy** 0 **Ionization Mode** ESI
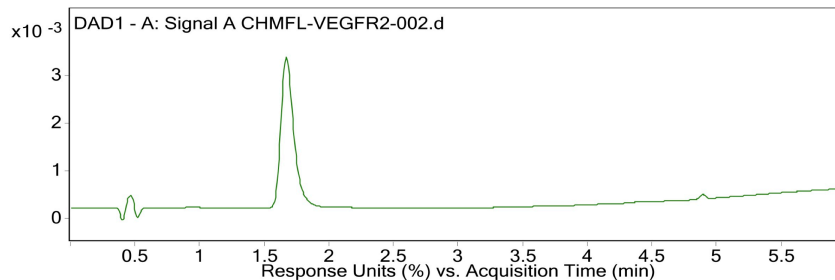
User Spectra

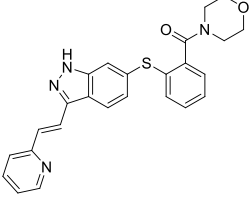**Fragmentor Voltage** 175 **Collision Energy** 0 **Ionization Mode** ESI

Peak List		
m/z	z	Abund
268.0554	1	427822.53
310.0669	1	820443.13
311.0685	1	172369.78
341.1107	1	4633917
341.2767		276697.25
342.1116	1	936843.44
343.1079	1	324462.28
396.8046	2	222896.53
681.2097	1	343195.19
682.212	1	136437.56
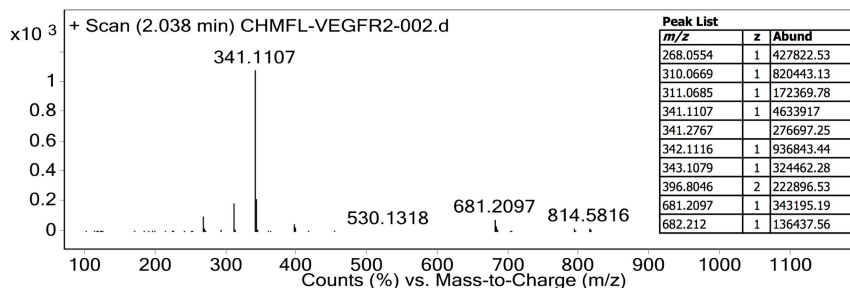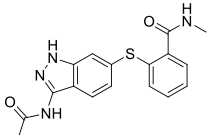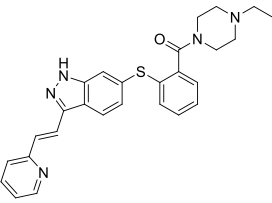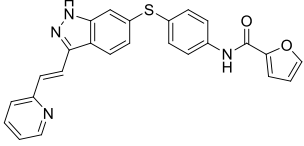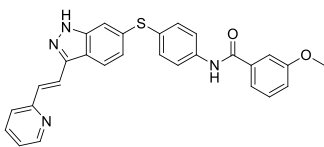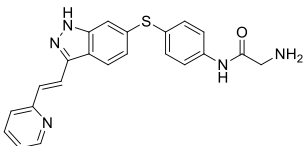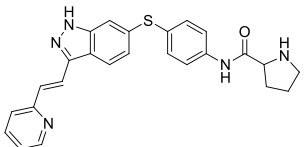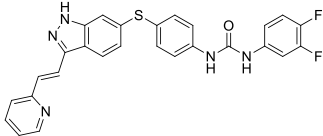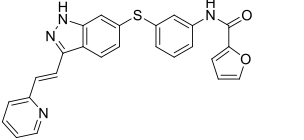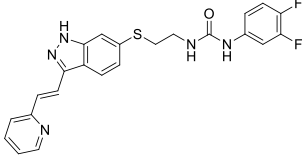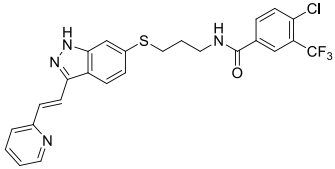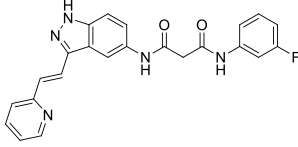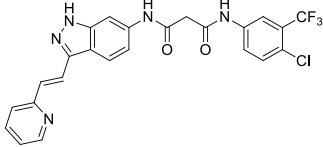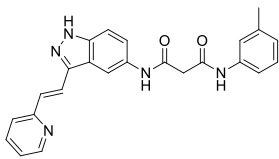
Figure S3 The LC-MS spectrum of CHMFL-VEGFR2-002.

Table S1 Anti-proliferative activity (GI_{50}) test in engineered BaF3 cells.

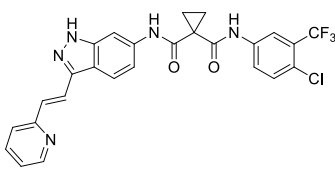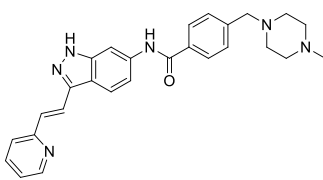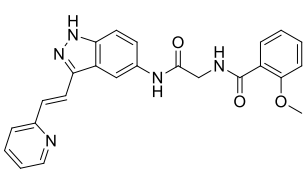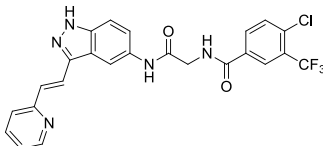| Compound	Structure	GI_{50} (µmol/L)			
		BaF3	TEL-VEGFR1-BaF3	TEL-VEGFR2-BaF3	TEL-VEGFR3-BaF3
1 (CHMFL-VEGFR2-002)		> 10	> 10	0.15	> 10
2		> 10	1.5	0.25	3.6
3		7.9	1.3	0.39	2.6
4		3.05	2.7	0.5	3.8
5		3.73	1.1	0.2	> 10
6		3.39	2.29	0.19	2.89
7		2.99	4.38	0.61	2.19
8		2.48	1.02	0.38	3.19

9		4.27	4.2	0.5	3.3
10		> 10	0.36	0.15	0.96
11		> 10	0.35	0.19	0.93
12		> 10	0.3	0.33	2
13		7.4	0.5	0.12	1.2
14		> 10	1	0.18	2
15		> 10	> 10	1.5	> 10
16		0.59	0.55	0.19	0.67
17		> 10	2.0	0.73	4.5
18		> 10	1.1	0.75	2.9

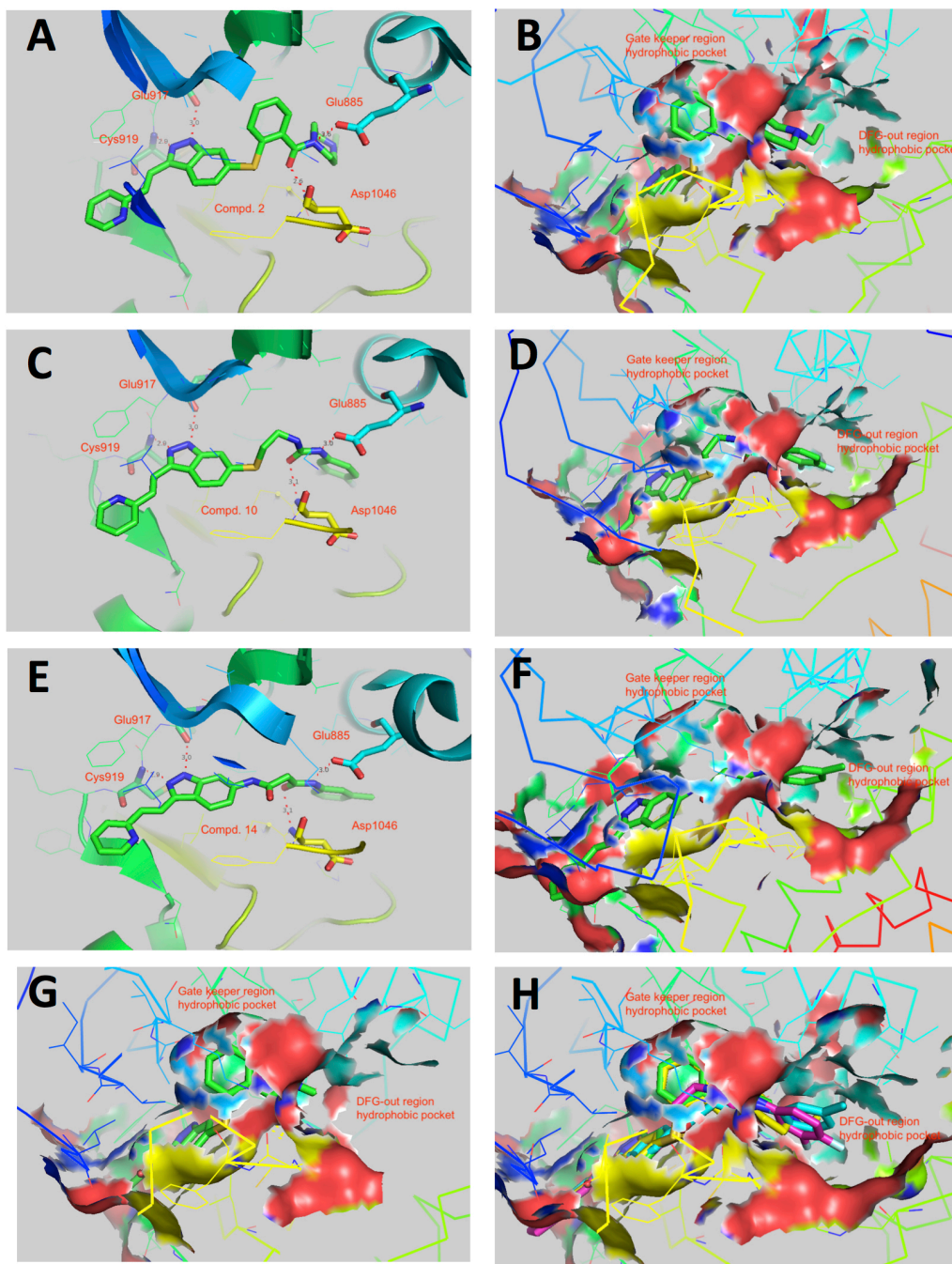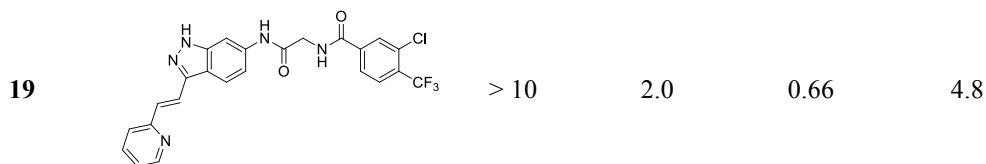| 19 | | > 10 | 2.0 | 0.66 | 4.8 |

Figure S4 Docking analysis of compounds **2**, **10**, **14** and CHMFL-VEGFR2-002. (A), (C) and (E) Cartoon mode illustration of compounds **2**, **10** and **14** in complex with

VEGFR2 kinase (PDB ID: 4AG8). (B), (D), (F) and (G) Solid surface illustration of two important hydrophobic pockets including the gate keeper region and the DFG-out region. (H) Overlapping of compounds **2**, **10**, **14** and CHMFL-VEGFR2-002 in the hydrophobic pocket with solid surface illustration mode.
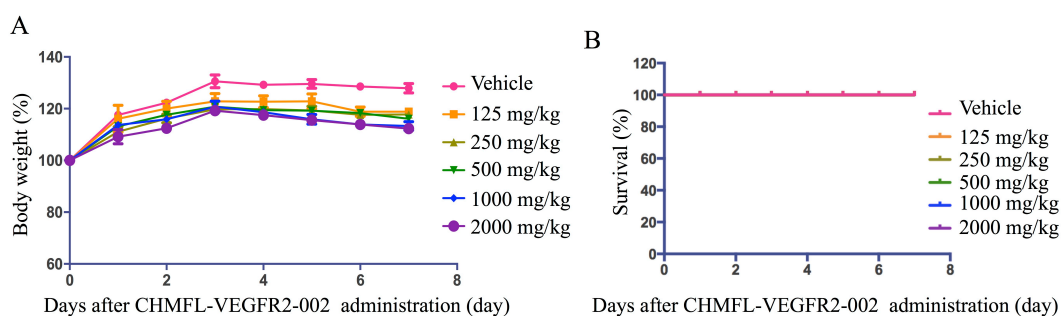

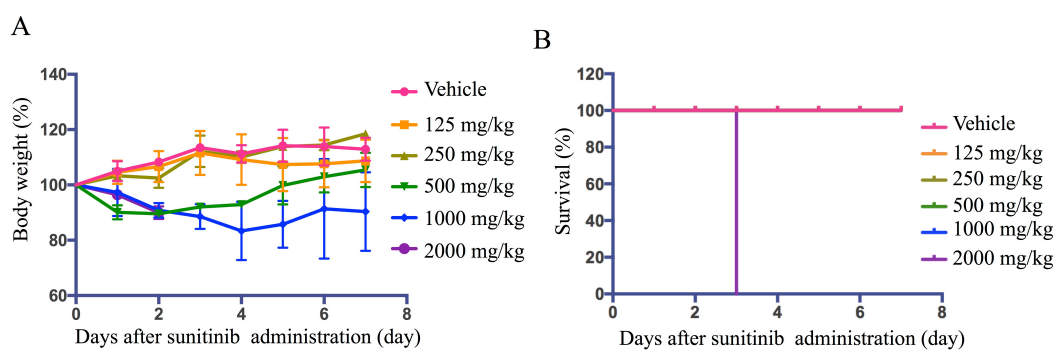**Figure S5** Acute toxicity test of CHMFL-VEGFR2-002.

Figure S6 Acute toxicity test of sunitinib.