

SUPPORTING INFORMATION

Title: Multigram-Scale Synthesis of the Nav1.7 Inhibitor GDC-0310

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Yanfang Zhao^{1*}

¹H NMR, ¹³C NMR, MS, Infrared and HPLC Spectra

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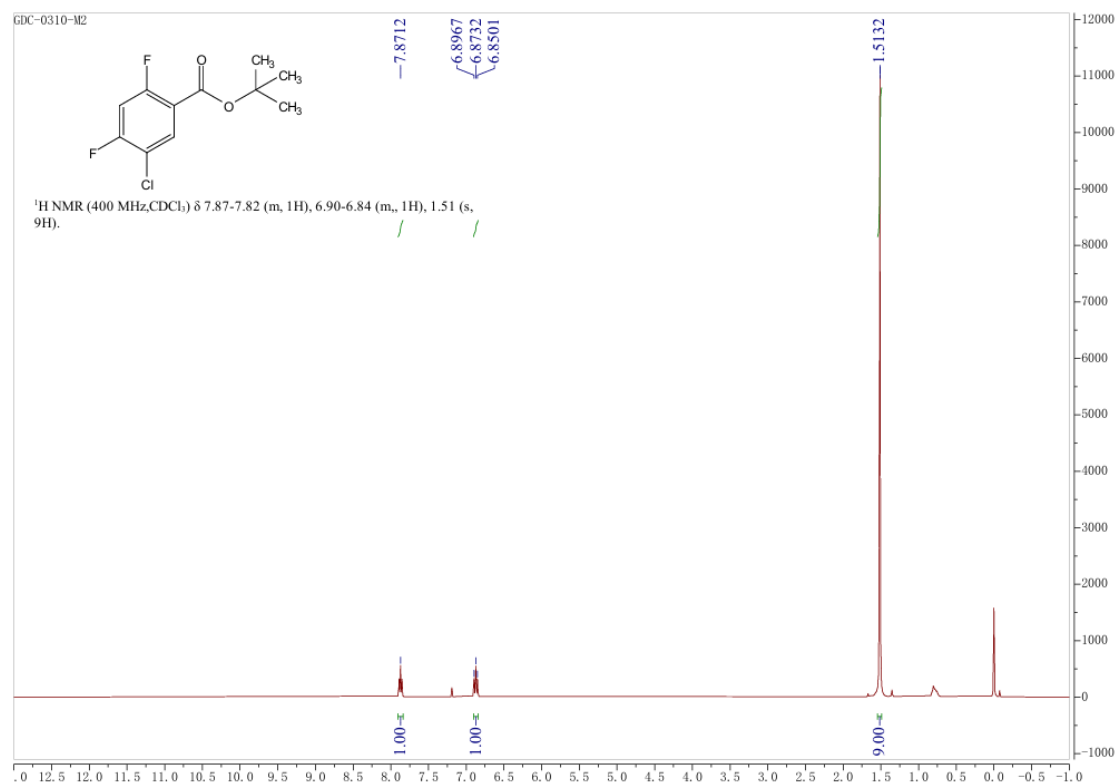


Fig. S1 ¹H NMR Spectrum of *tert*-butyl-5-chloro-2,4-difluorobenzoate (**2**)

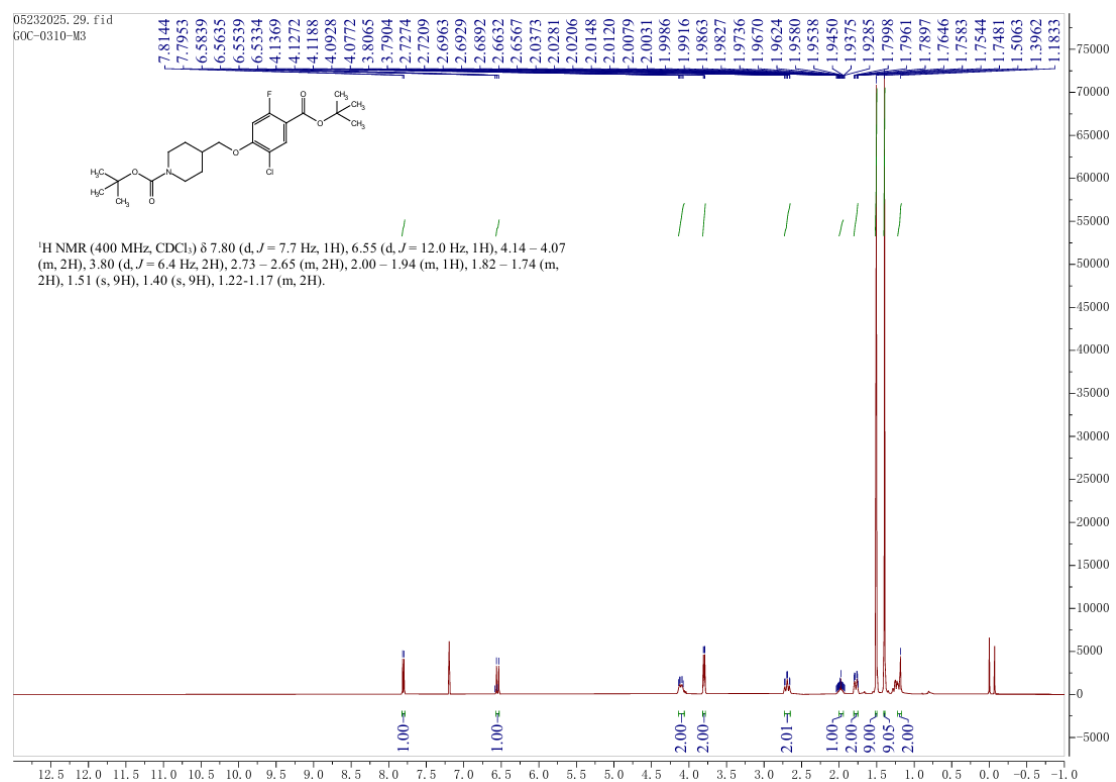


Fig. S2 ¹H NMR Spectrum of *tert*-butyl-4-((4-(*tert*-butoxycarbonyl)-2-chloro-5-fluorophenoxy)methyl)piperidine-1-carboxylate (**3**)

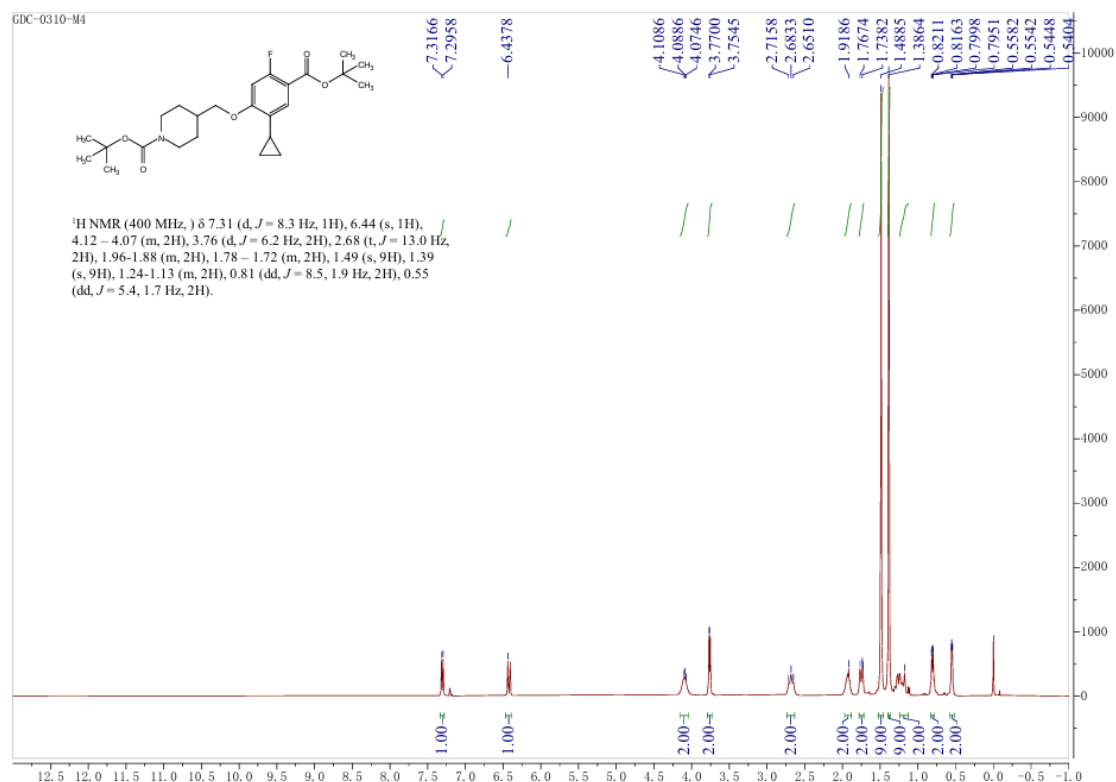


Fig. S3 ¹H NMR Spectrum of *tert*-butyl-4-((1-(*tert*-butoxycarbonyl)piperidin-4-yl)methoxy)-5-cyclopropyl-2-fluorobenzoate (**4**)

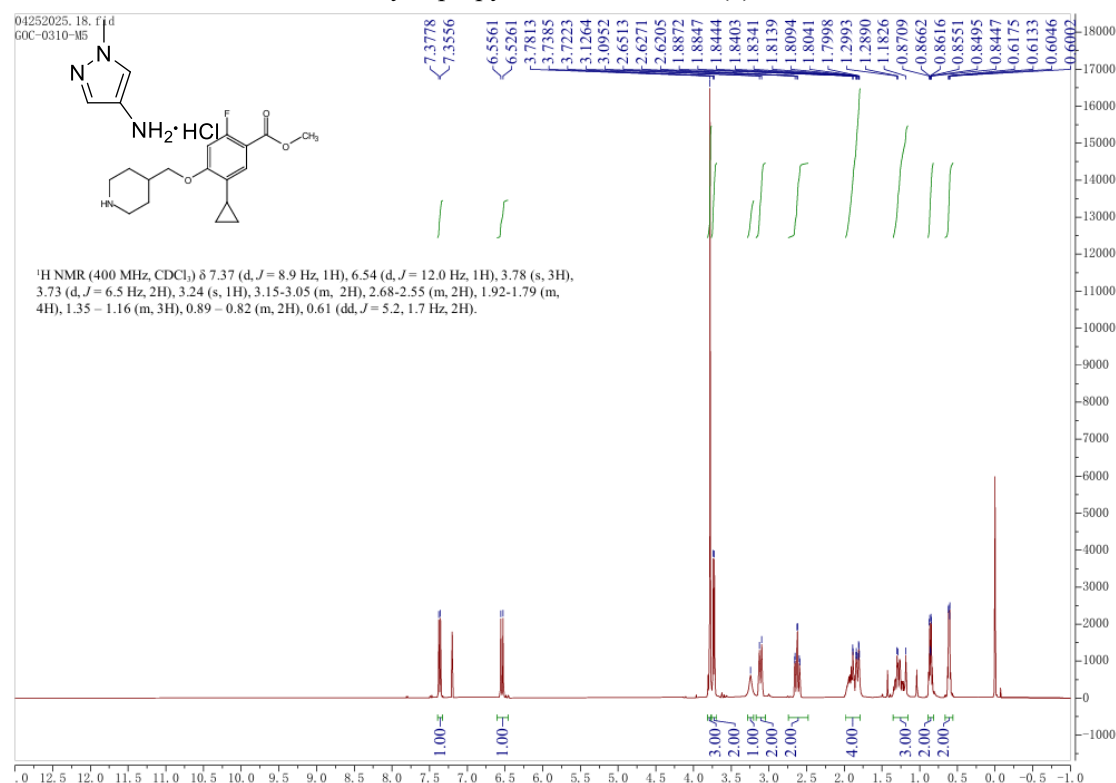


Fig. S4 ¹H NMR Spectrum of methyl-5-cyclopropyl-2-fluoro-4-(piperidin-4-ylmethoxy)benzoate hydrochloride (**5**)

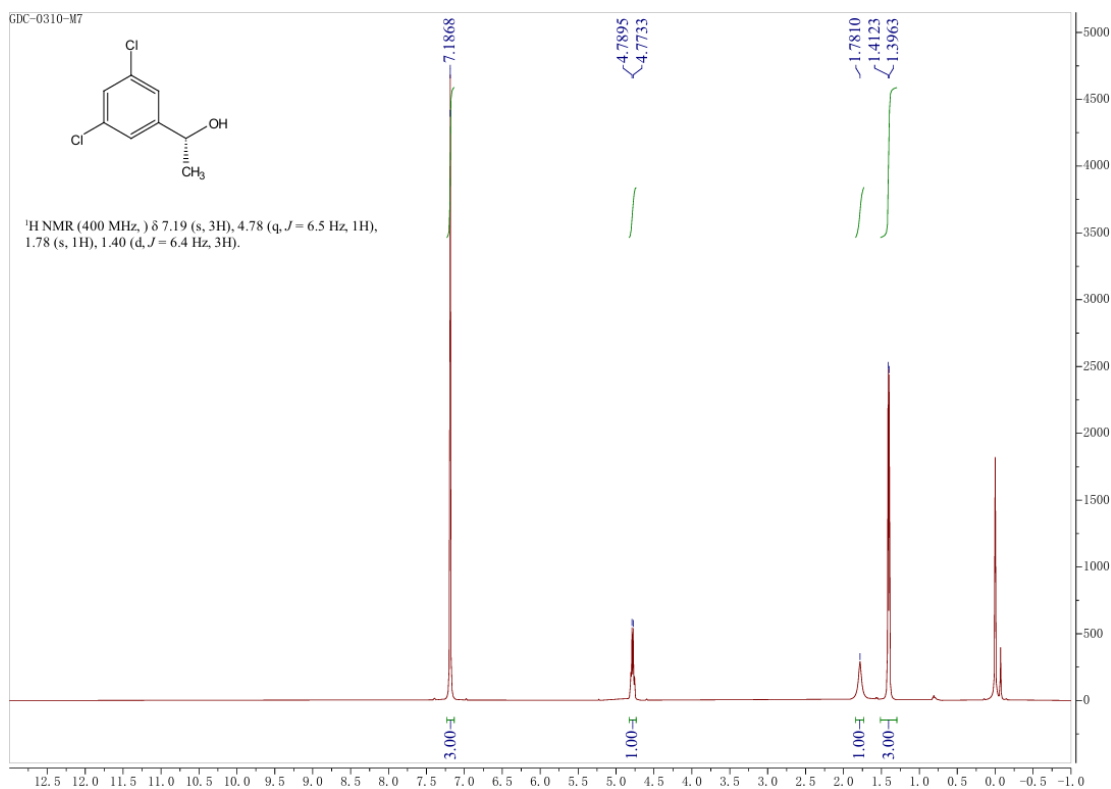


Fig. S5 ¹H NMR Spectrum of (*R*)-1-(3,5-Dichlorophenyl)ethan-1-ol (**7**)

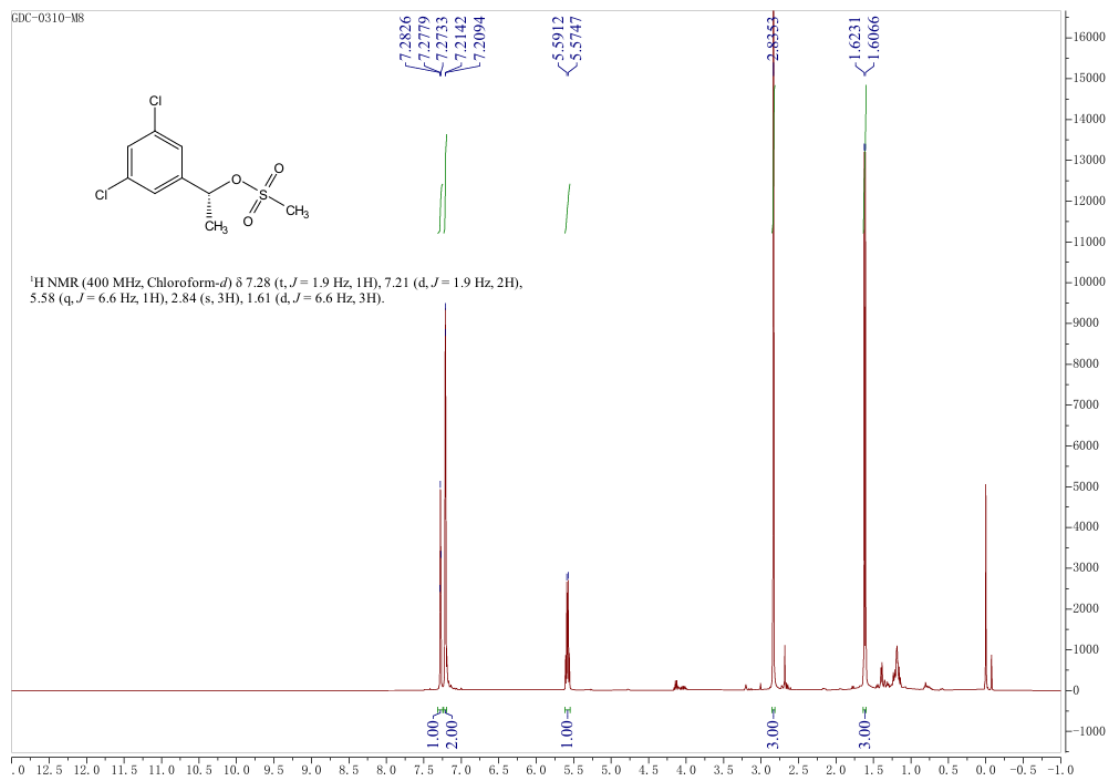


Fig. S6 ¹H NMR Spectrum of (*R*)-1-(3,5-Dichlorophenyl)ethyl methanesulfonate (**8**)

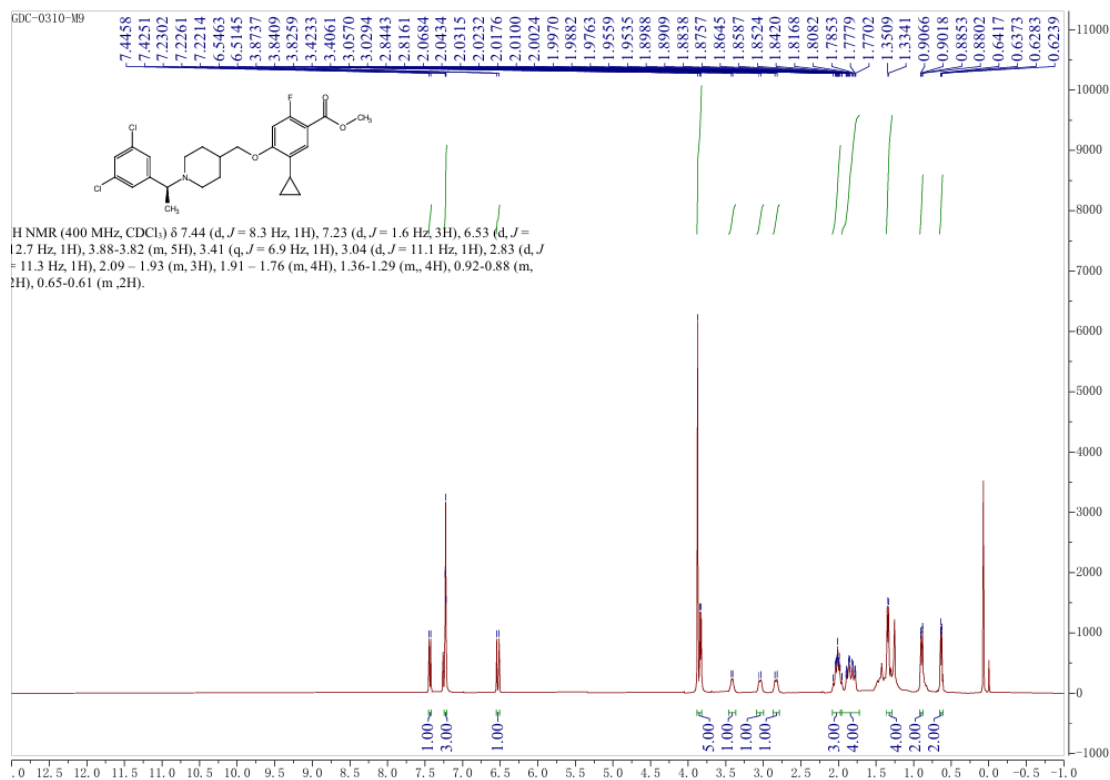


Fig. S7 ¹H NMR Spectrum of methyl (*S*)-5-cyclopropyl-4-((1-(1-(3,5-dichlorophenyl)ethyl)piperidin-4-yl)methoxy)-2-fluorobenzoate (**9**)

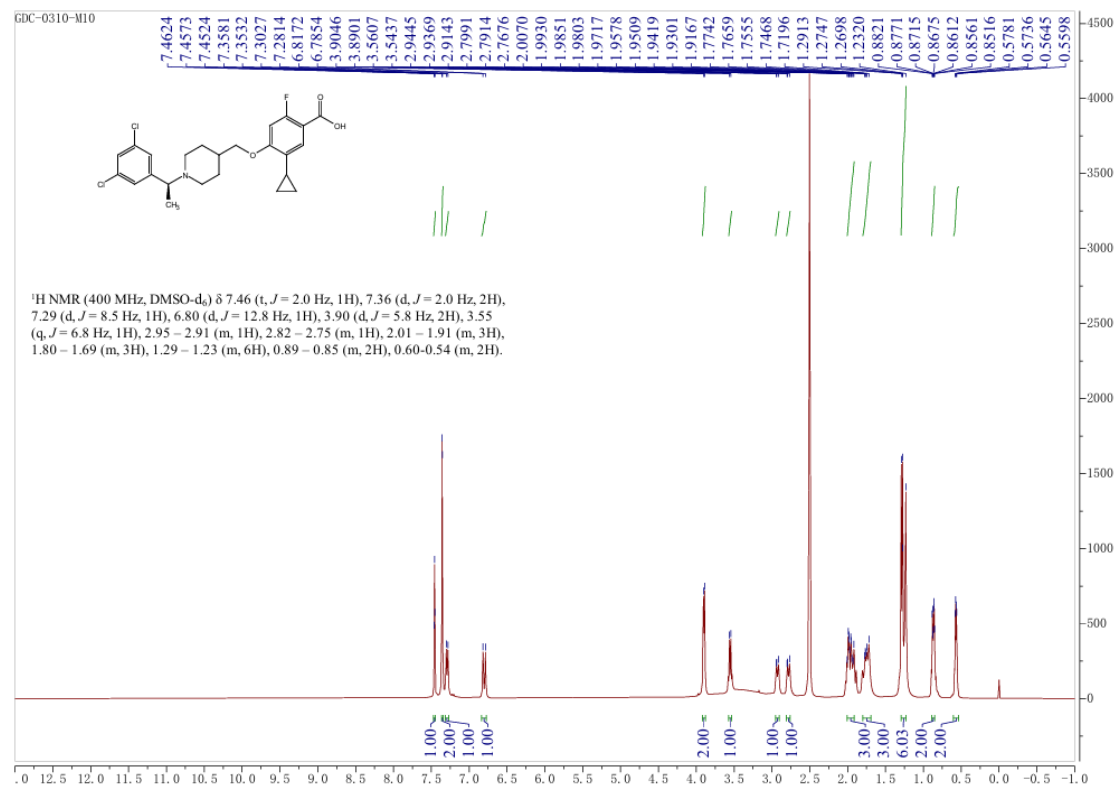


Fig. S8 ¹H NMR Spectrum of (*S*)-5-cyclopropyl-4-((1-(1-(3,5-dichlorophenyl)ethyl)piperidin-4-yl)methoxy)-2-fluorobenzoic acid (**10**)

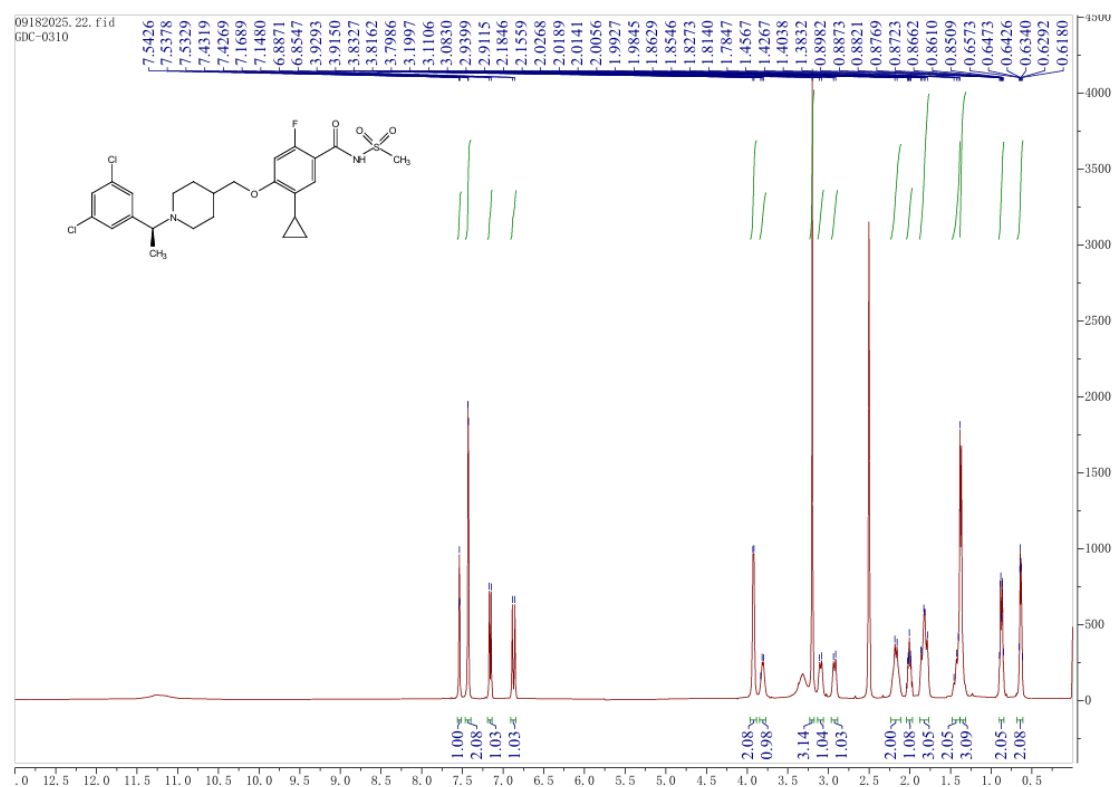


Fig. S9 ¹H NMR Spectrum of (S)-5-cyclopropyl-4-((1-(3,5-dichlorophenyl)ethyl)piperidin-4-yl)methoxy)-2-fluoro-N-(methylsulfonyl)benzamide (GDC-0310)

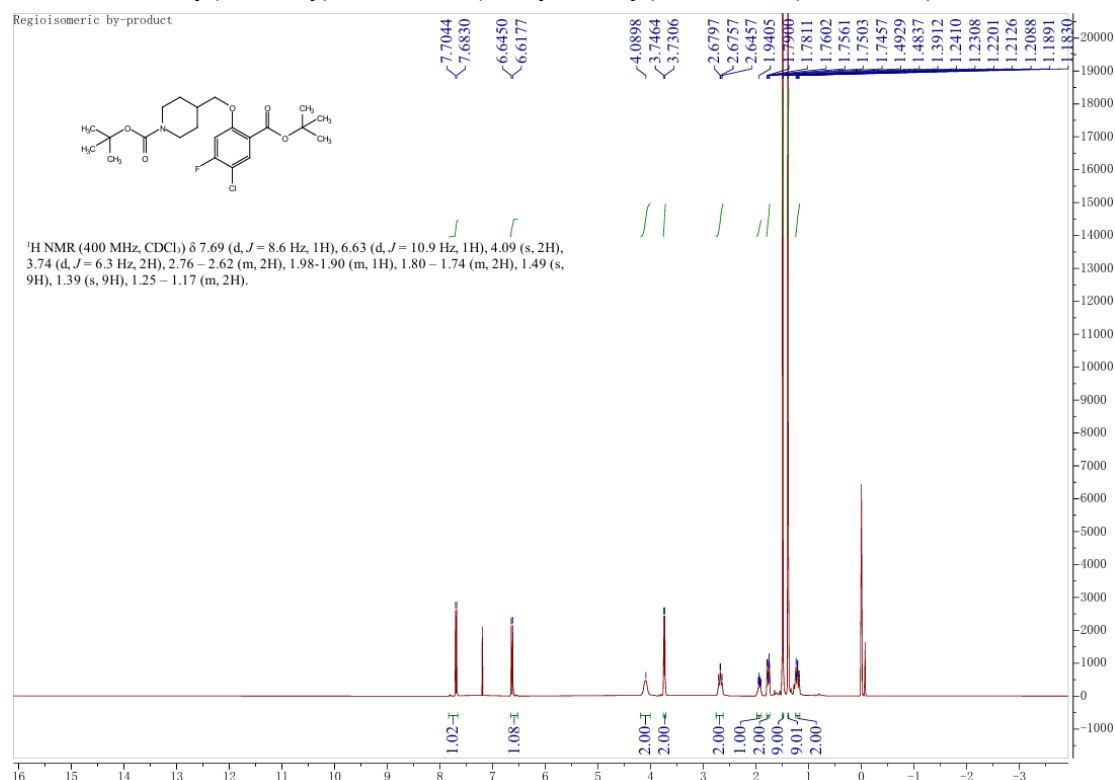


Fig. S10 ¹H NMR Spectrum of regioisomeric by-product

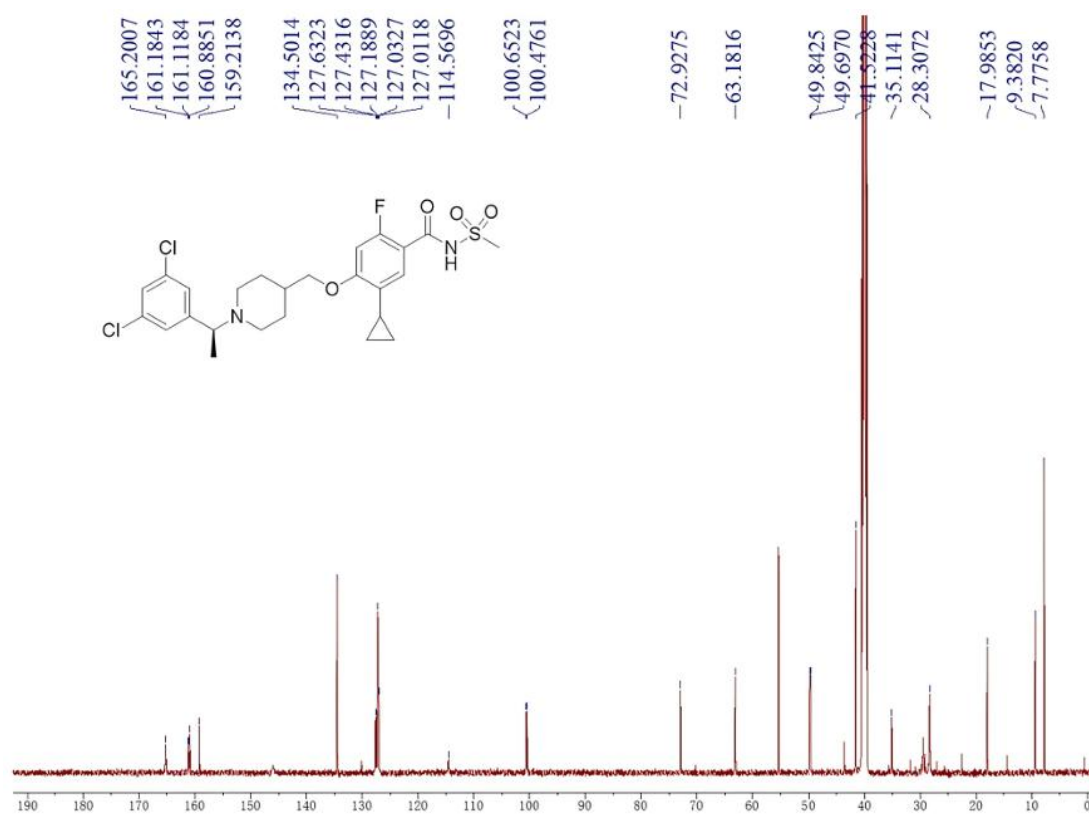


Fig. S11 ¹³C NMR Spectrum of (*S*)-5-cyclopropyl-4-((1-(1-(3,5-dichlorophenyl)ethyl)piperidin-4-yl)methoxy)-2-fluoro-N-(methylsulfonyl)benzamide (**GDC-0310**)

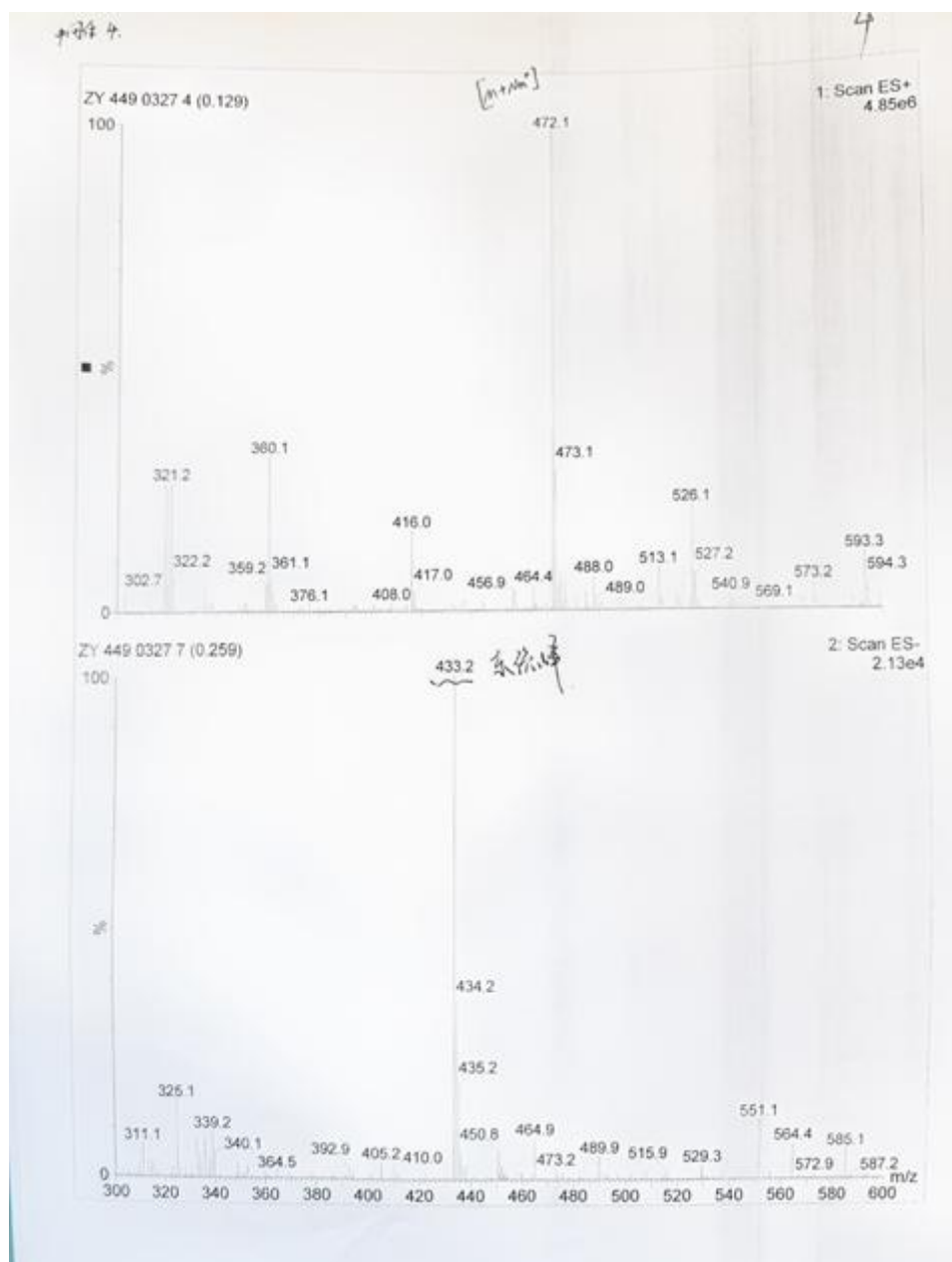


Fig. S12 MS Spectrum of *tert*-butyl-4-((1-(*tert*-butoxycarbonyl)piperidin-4-yl)methoxy)-5-cyclopropyl-2-fluorobenzoate (**4**)

5.

5

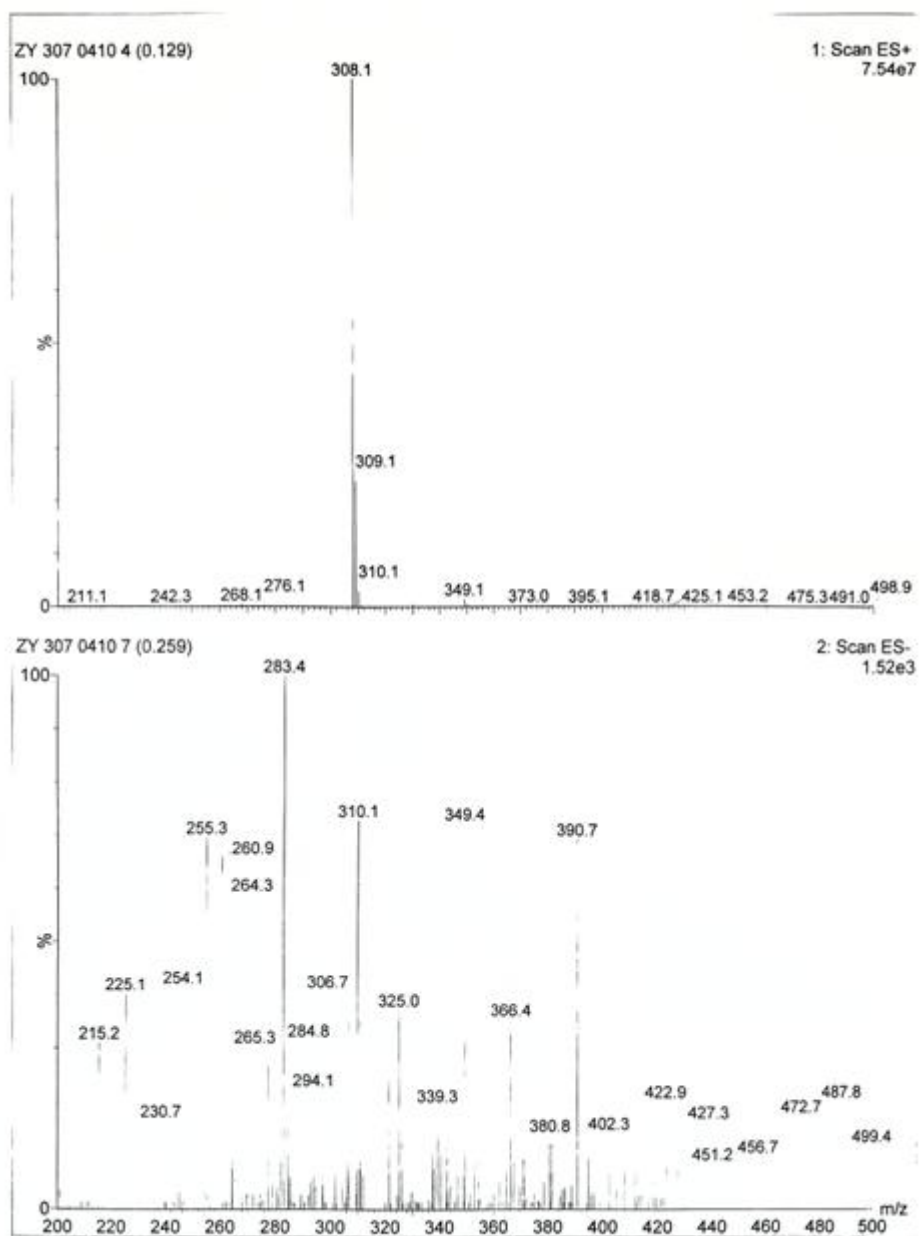


Fig. S13 MS Spectrum of methyl-5-cyclopropyl-2-fluoro-4-(piperidin-4-ylmethoxy)benzoate hydrochloride (**5**)

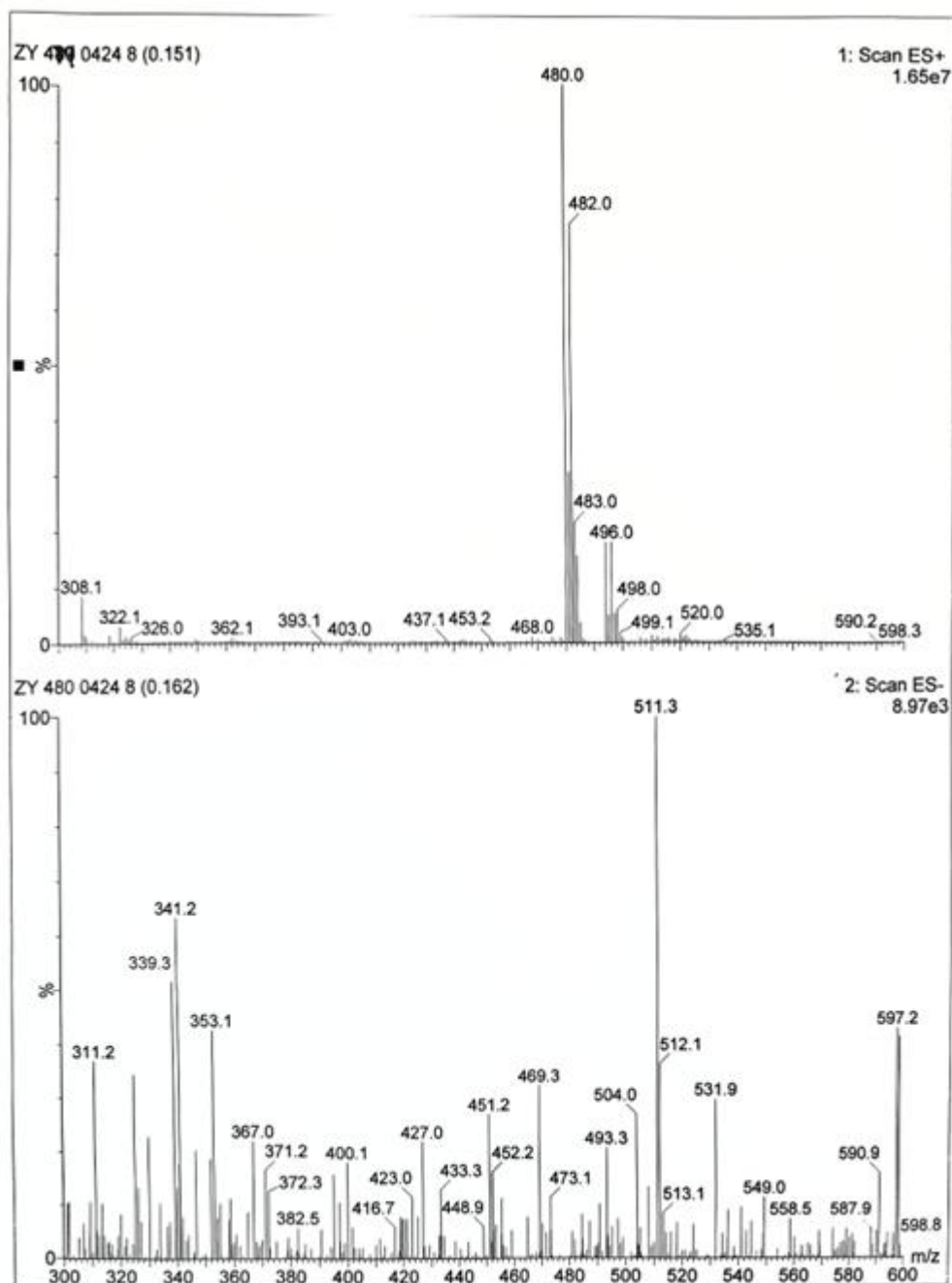


Fig. S14 MS Spectrum of methyl (*S*)-5-cyclopropyl-4-((1-(1-(3,5-dichlorophenyl)ethyl)piperidin-4-yl)methoxy)-2-fluorobenzoate (**9**)

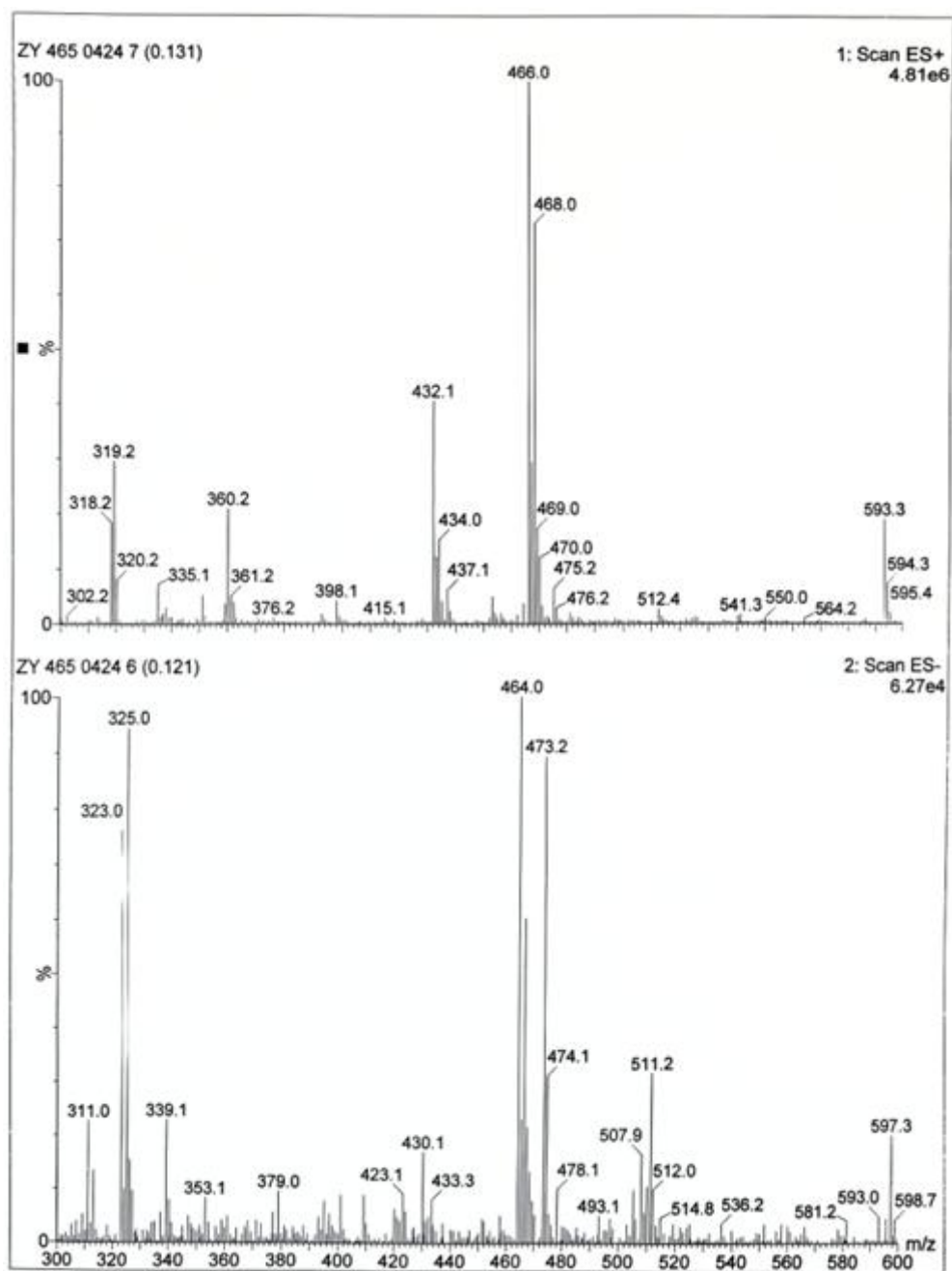


Fig. S15 MS Spectrum of (*S*)-5-cyclopropyl-4-((1-(1-(3,5-dichlorophenyl)ethyl)piperidin-4-yl)methoxy)-2-fluorobenzoic acid (**10**)

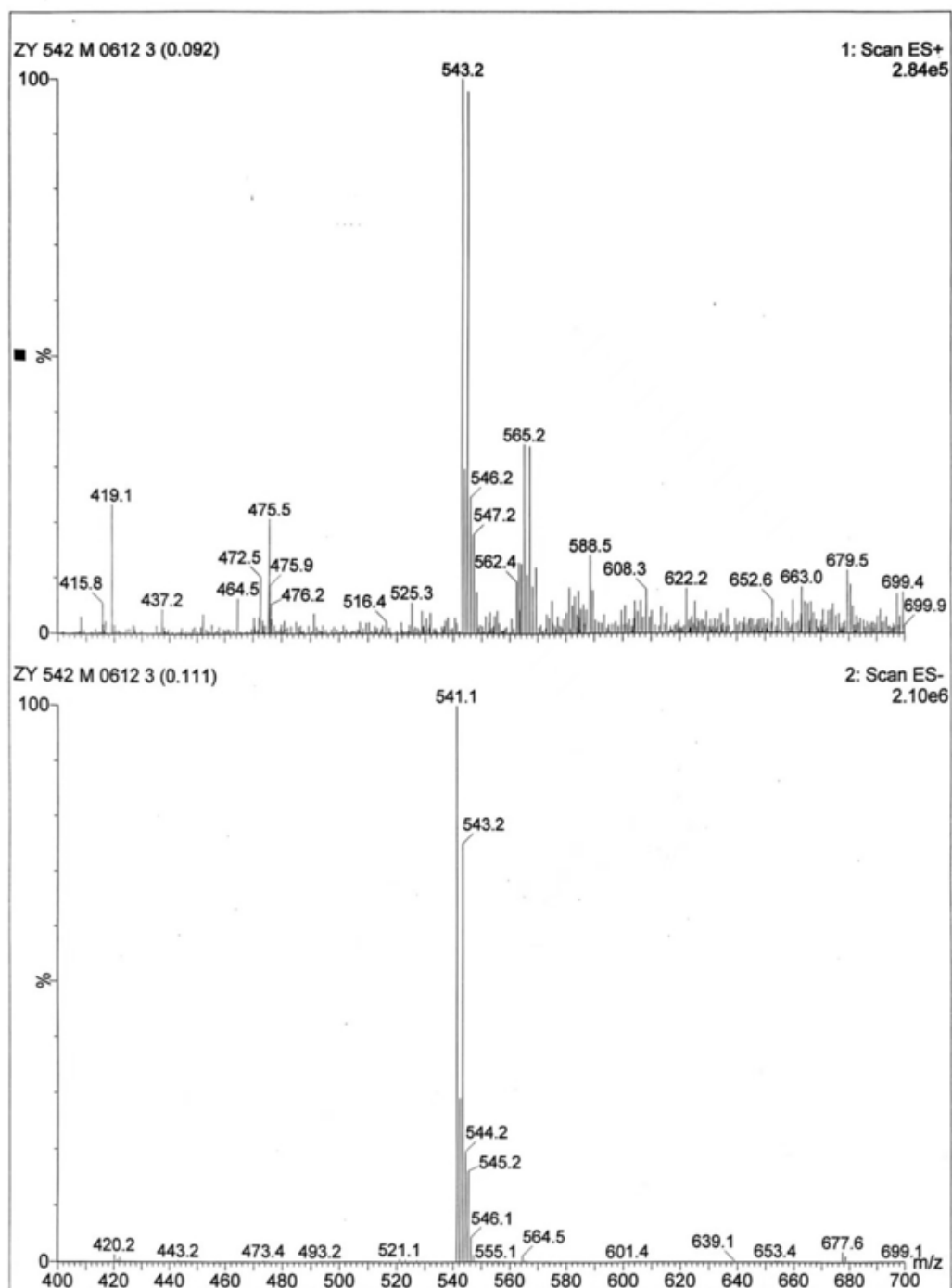
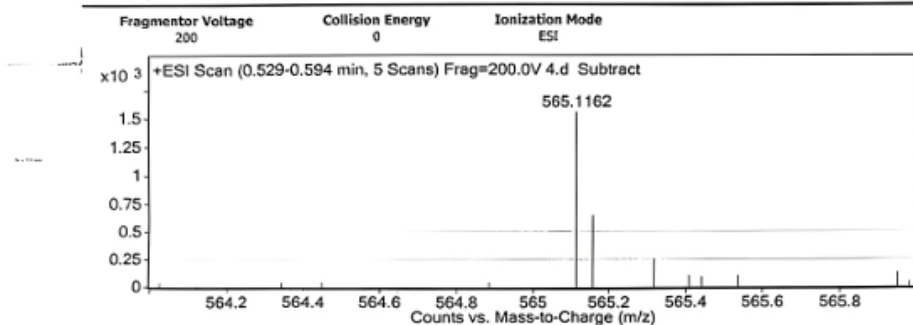


Fig. S16 MS Spectrum of (*S*)-5-cyclopropyl-4-((1-(1-(3,5-dichlorophenyl)ethyl)piperidin-4-yl)methoxy)-2-fluoro-N-(methylsulfonyl)benzamide (**GDC-0310**)

Qualitative Analysis Report

Data Filename	4.d	Sample Name	Sample18
Sample Type	Sample	Position	P1-C4
Instrument Name	Instrument 1	User Name	
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IRM Calibration Status	Success	DA Method	Default.m
Comment			
Sample Group		Info.	
Acquisition SW	6200 series TOF/6500 series		
Version	Q-TOF B.05.01 (B5125.2)		

User Spectra



Peak List

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418.7881	2	10587.3
419.2897	2	6290.33
475.3333	2	11369.77
475.8371	2	5332.28
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701.5033	1	10851.17
814.5895	1	5410.94

*** End Of Report ***

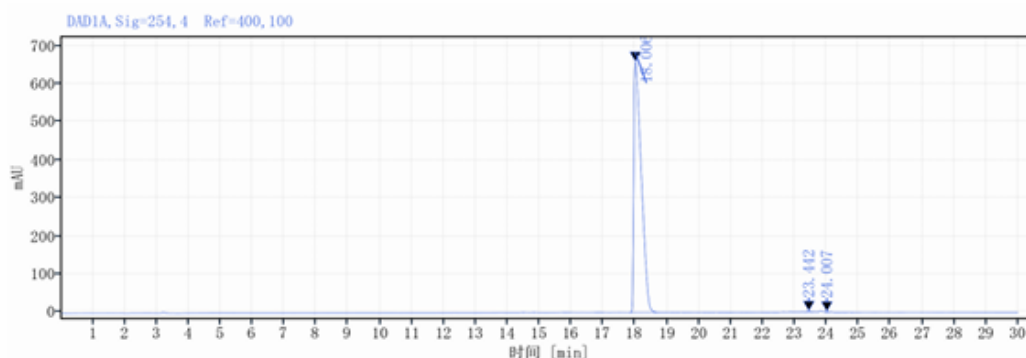
Fig. S17 HRMS Spectrum of (*S*)-5-cyclopropyl-4-((1-(1-(3,5-dichlorophenyl)ethyl)piperidin-4-yl)methoxy)-2-fluoro-N-(methylsulfonyl)benzamide (**GDC-0310**)

单次进样报告



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数据文件: 2026-05-26 10-43-42+08-00-03. dx
 序列名称: 2026-05-26 08-52-04+08-00 项目名称: TEST
 样品名称: GDC-0310-Z 操作者: 系统
 仪器: 1200 进样日期: 2026-05-26 10:45:15+08:00
 进样体积: 5.000 位置: 52
 采集方法: LC-M. amx 类型: 样品
 处理方法: GC_LC 面积百分比_DefaultMethod. pmx 样品含量: 0.00
 手动修改: 手动积分



信号: DAD1A, Sig=254, 4 Ref=400, 100

Retention Time[min]	Type	Peak Width[min]	Peak Area	Peak Height	Peak Area%
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23.442	VV	0.28	19.25	3.12	0.18
24.007	VV	0.14	12.65	2.38	0.12
总和			10831.99		

Fig. S18 HPLC Spectrum of (*S*)-5-cyclopropyl-4-((1-(1-(3,5-dichlorophenyl)ethyl)piperidin-4-yl)methoxy)-2-fluoro-N-(methylsulfonyl)benzamide (**GDC-0310**)

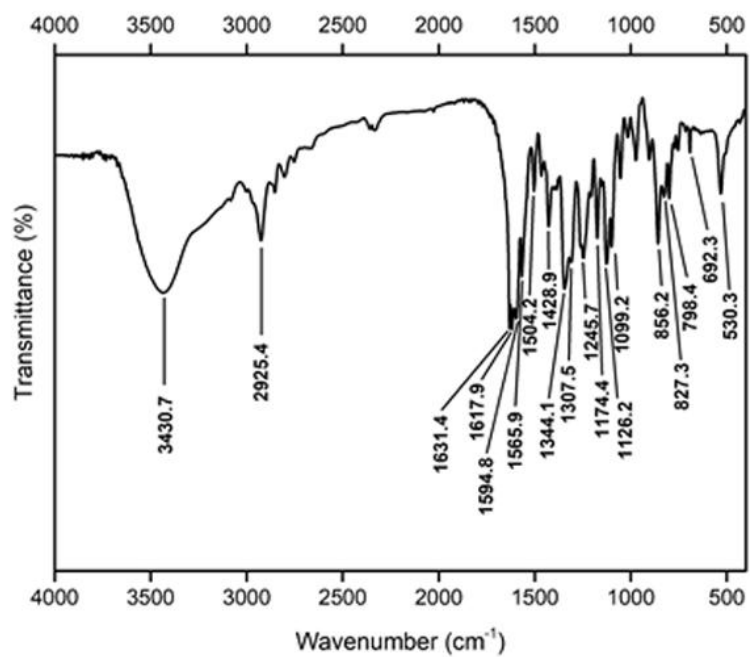


Fig. S19 Infrared Spectrum of (*S*)-5-cyclopropyl-4-((1-(1-(3,5-dichlorophenyl)ethyl)piperidin-4-yl)methoxy)-2-fluoro-*N*-(methylsulfonyl)benzamide (**GDC-0310**)