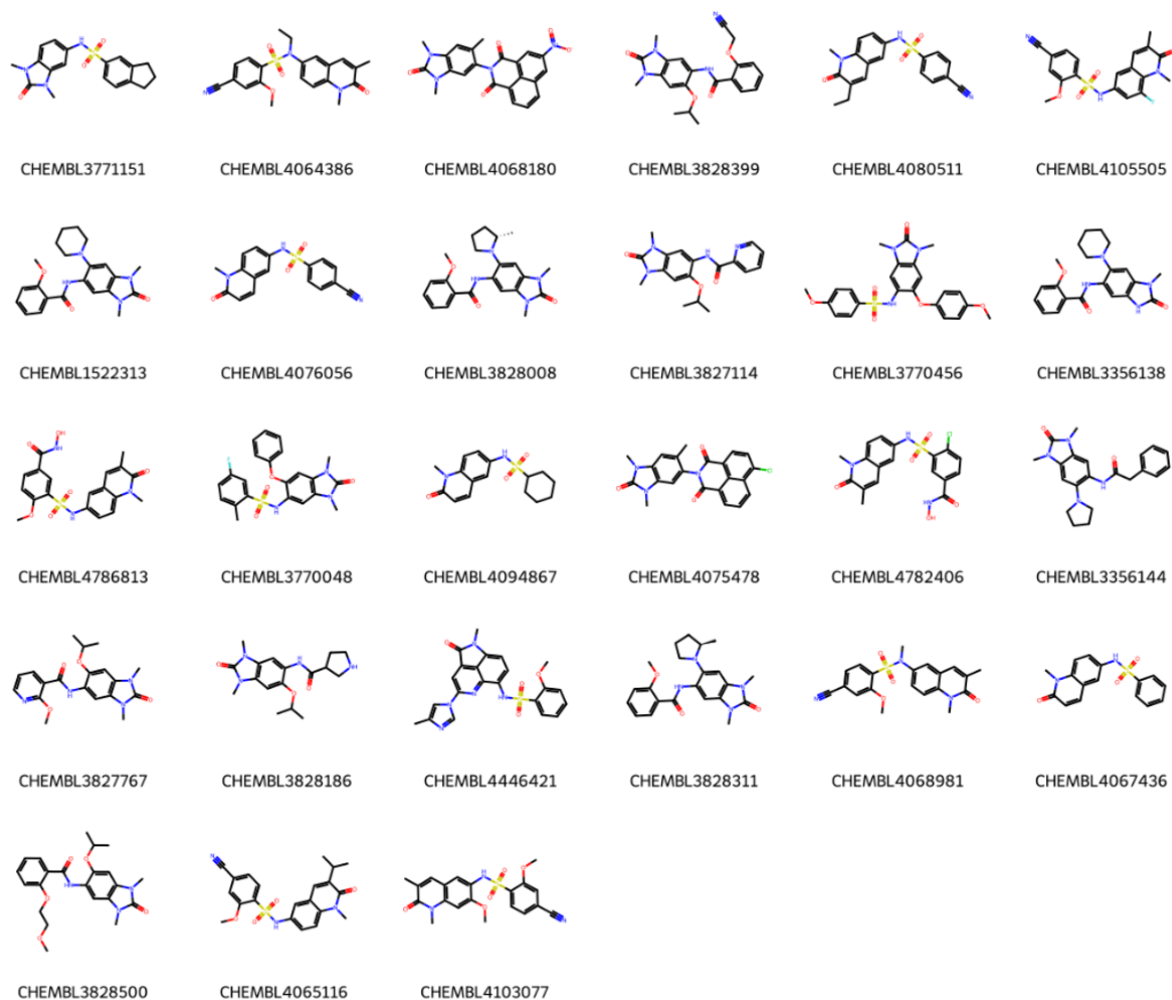


Accelerating BRPF1b hit identification with BioPhysical and Active Learning Screening (*BioPALS*)

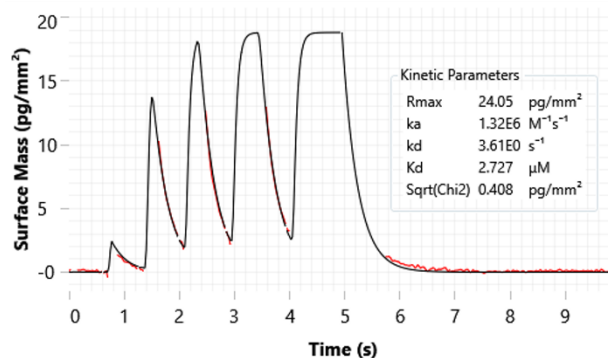
Sandeep Pal,^{#[a]} Zandile Nare,^{#[a]} Vincenzo A. Rao,^[a] Brian O. Smith,^[b] Ian Morrison,^[a] Edward A. Fitzgerald,^[c] Andrew Scott,^[a] Matilda J. Bingham^[a] and Thomas Pesnot^{*[a]}

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Supplementary Information



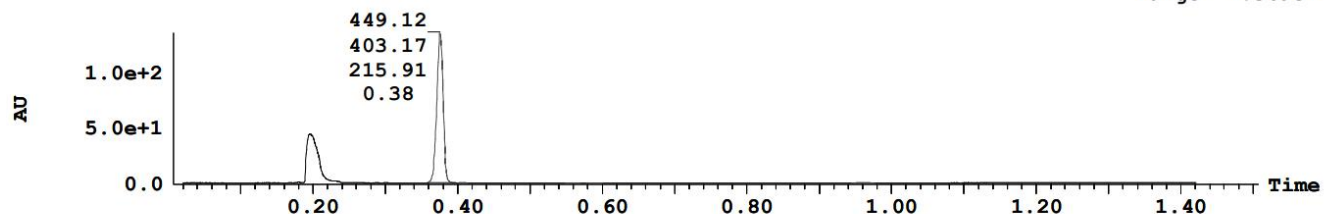
Supplementary Figure 1: Chemical structure of the 27 known BRPF1b inhibitors used for the similarity search.



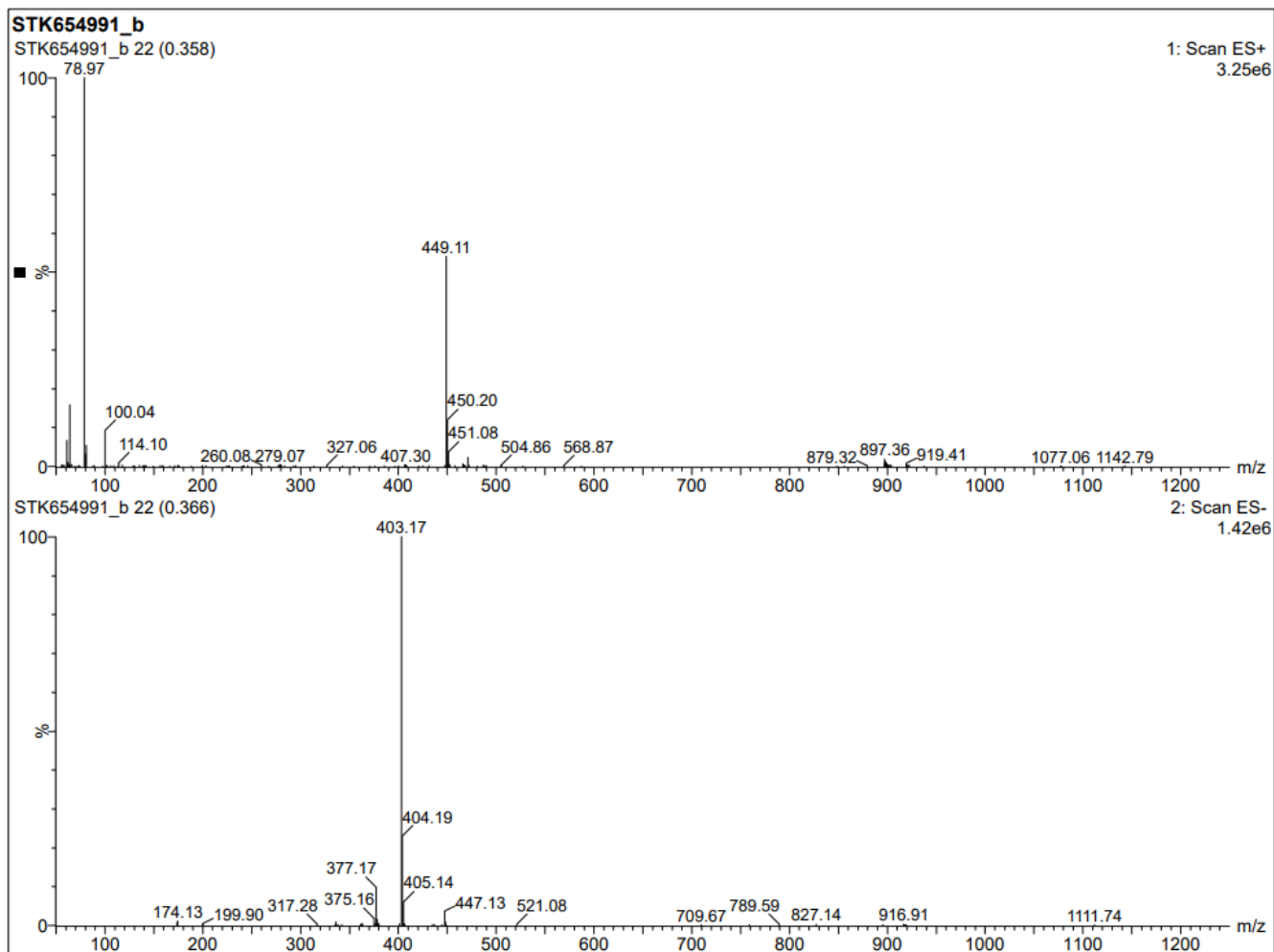
Supplementary Figure 2: Representative waveRAPID[®] sensorgram for GSK6853 binding to BRPF1a with indicated kinetic and fitting parameters.

3: UV Detector: TAC: Wavelength Range: (210 - 350)

1.366e+2
Range: 1.369e+2



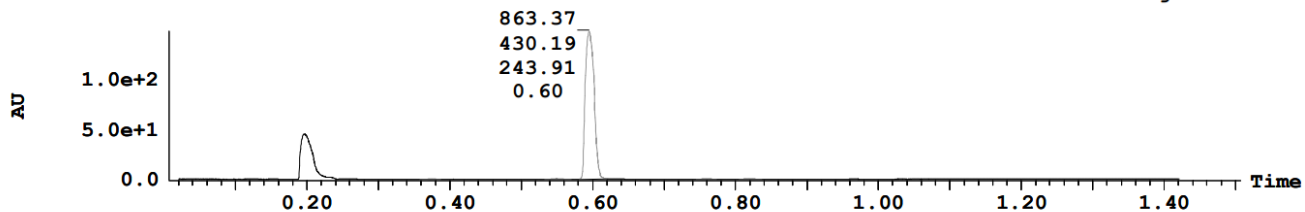
Peak Number	Time	Area %Total	AreaAbs
2	0.38	99.25	1388324.9
3	0.41	0.17	2423.0
5	0.56	0.10	1402.8
6	0.59	0.13	1820.2
9	0.96	0.35	4884.8



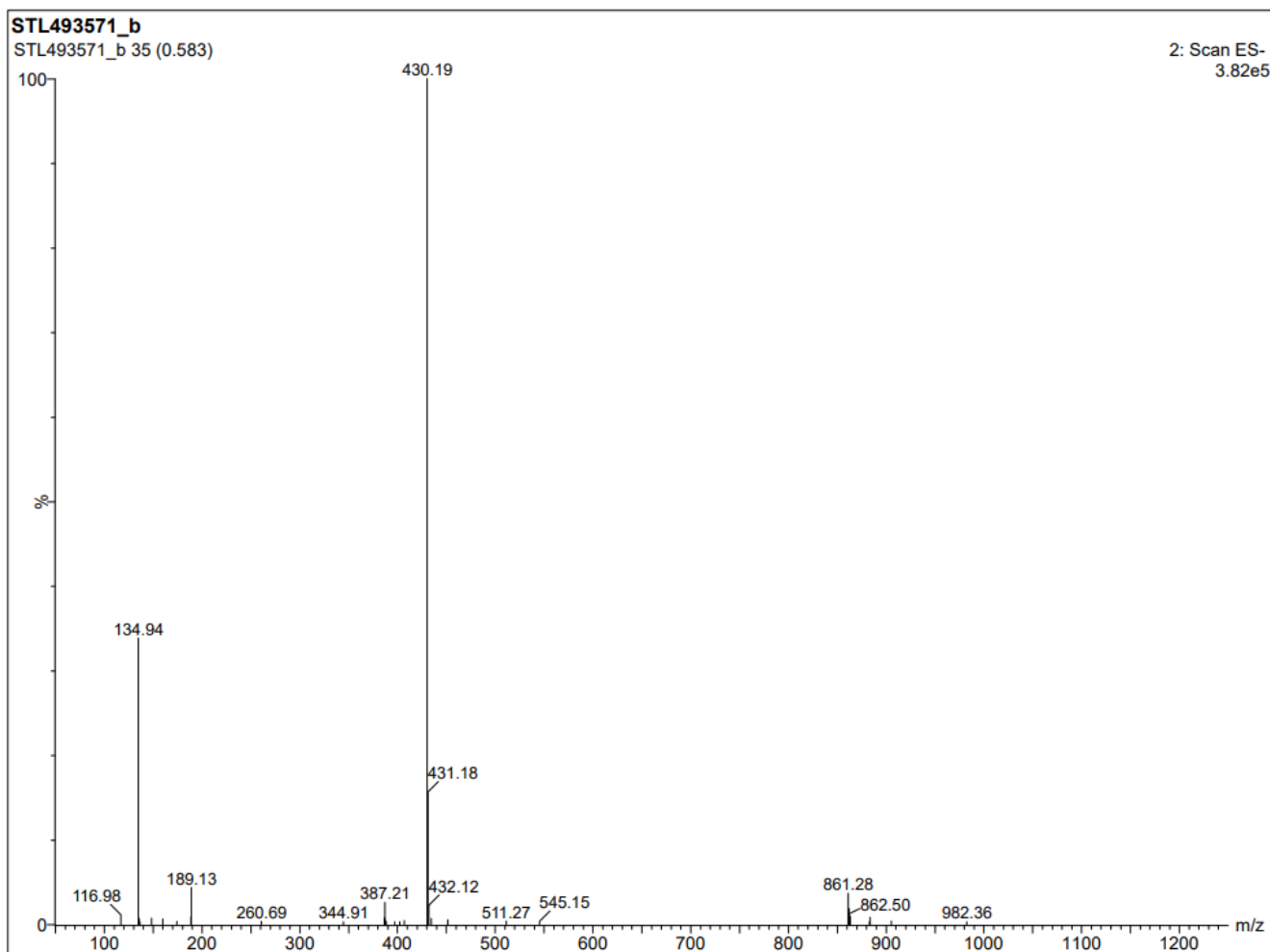
Supplementary Figure 3: LCMS purity of compound 2.

3: UV Detector: TAC: Wavelength Range: (210 - 350)

1.471e+2
Range: 1.474e+2



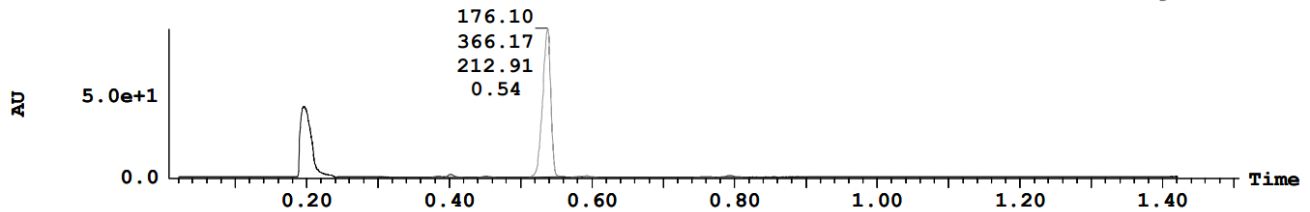
Peak Number	Time	Area %Total	AreaAbs
3	0.38	0.22	4595.4
5	0.55	0.51	10754.9
6	0.60	98.82	2088477.4
7	0.76	0.16	3316.9
8	0.82	0.30	6344.9



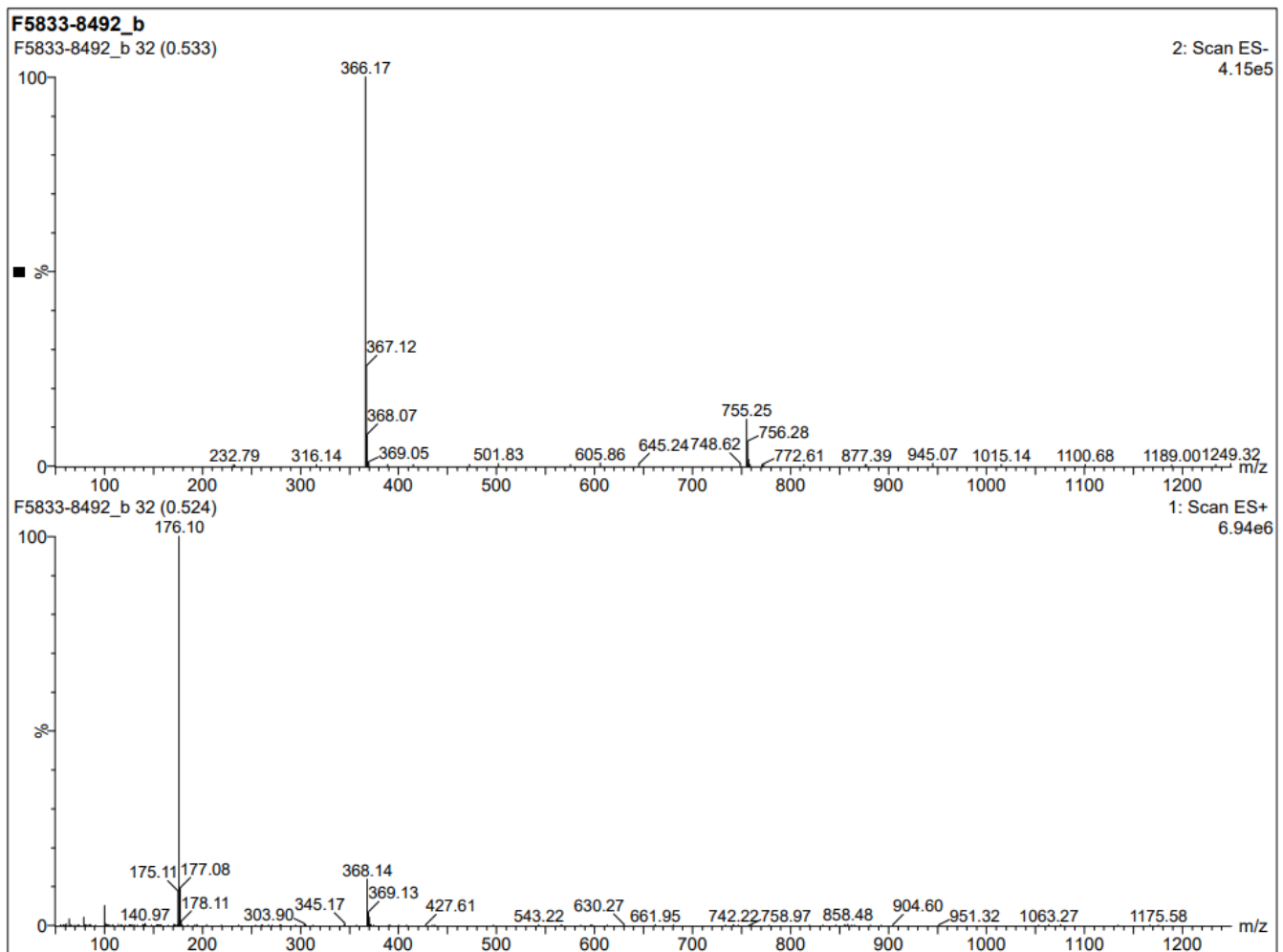
Supplementary Figure 4: LCMS purity of compound 3.

3: UV Detector: TAC: Wavelength Range: (210 - 350)

9.134e+1
Range: 9.164e+1



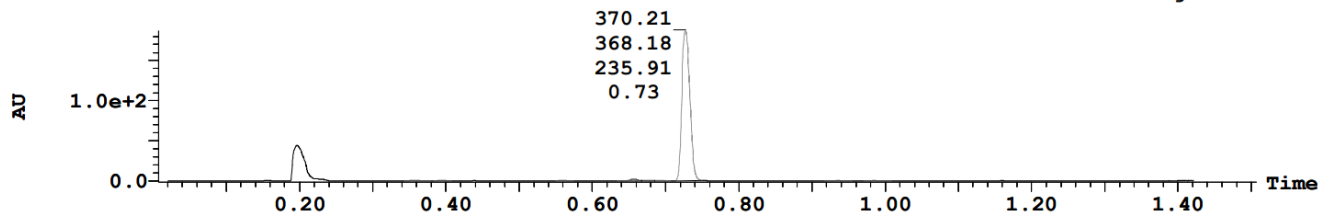
Peak Number	Time	Area %Total	AreaAbs
3	0.38	0.43	5414.1
4	0.40	1.32	16644.7
5	0.45	0.44	5521.7
7	0.54	95.93	1209802.3
8	0.58	0.27	3435.4
9	0.59	0.66	8306.7
12	0.76	0.12	1540.0
13	0.79	0.83	10462.8



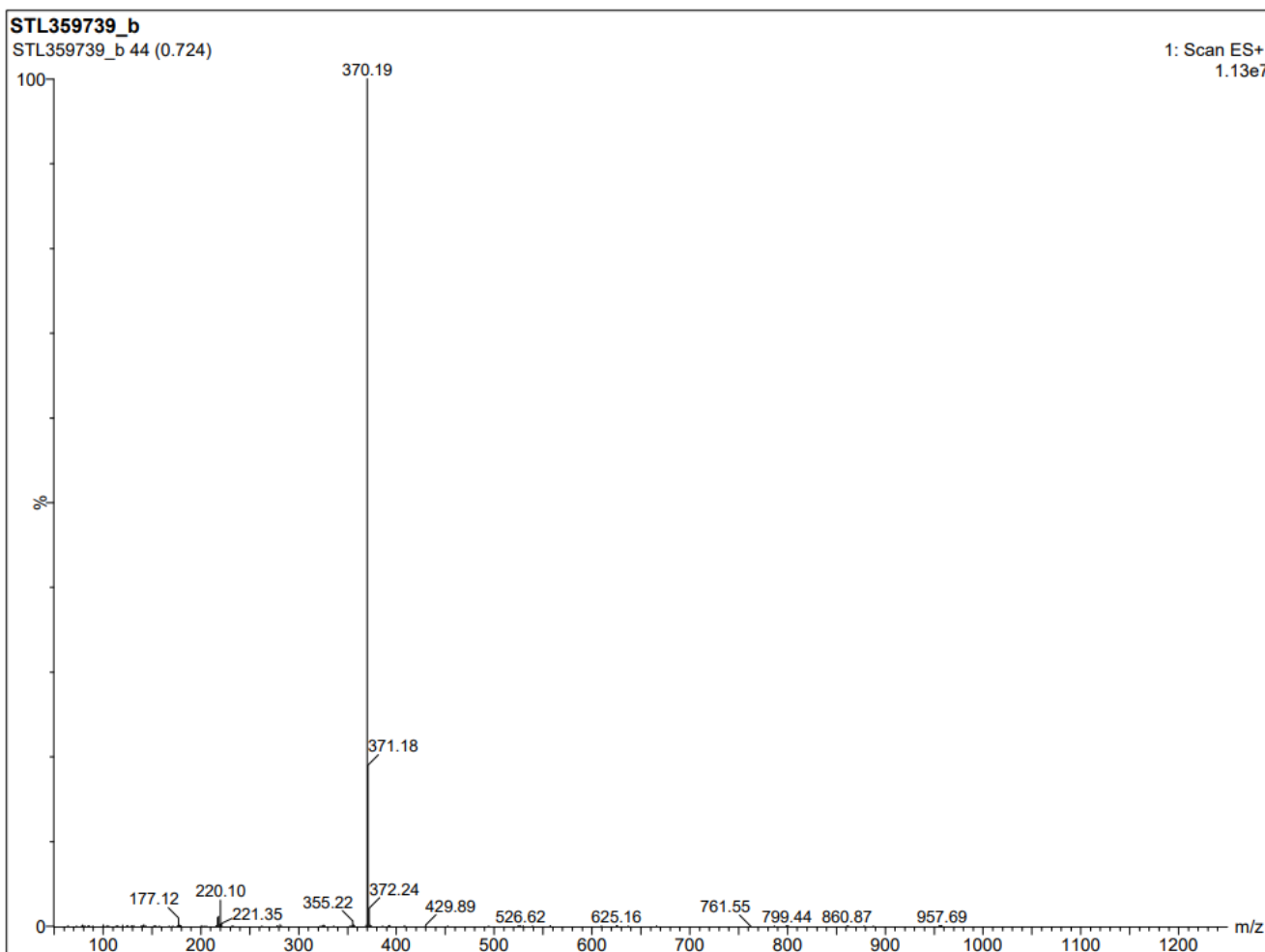
Supplementary Figure 5: LCMS purity of compound 4.

3: UV Detector: TAC: Wavelength Range: (210 - 350)

1.87e+2
Range: 1.871e+2



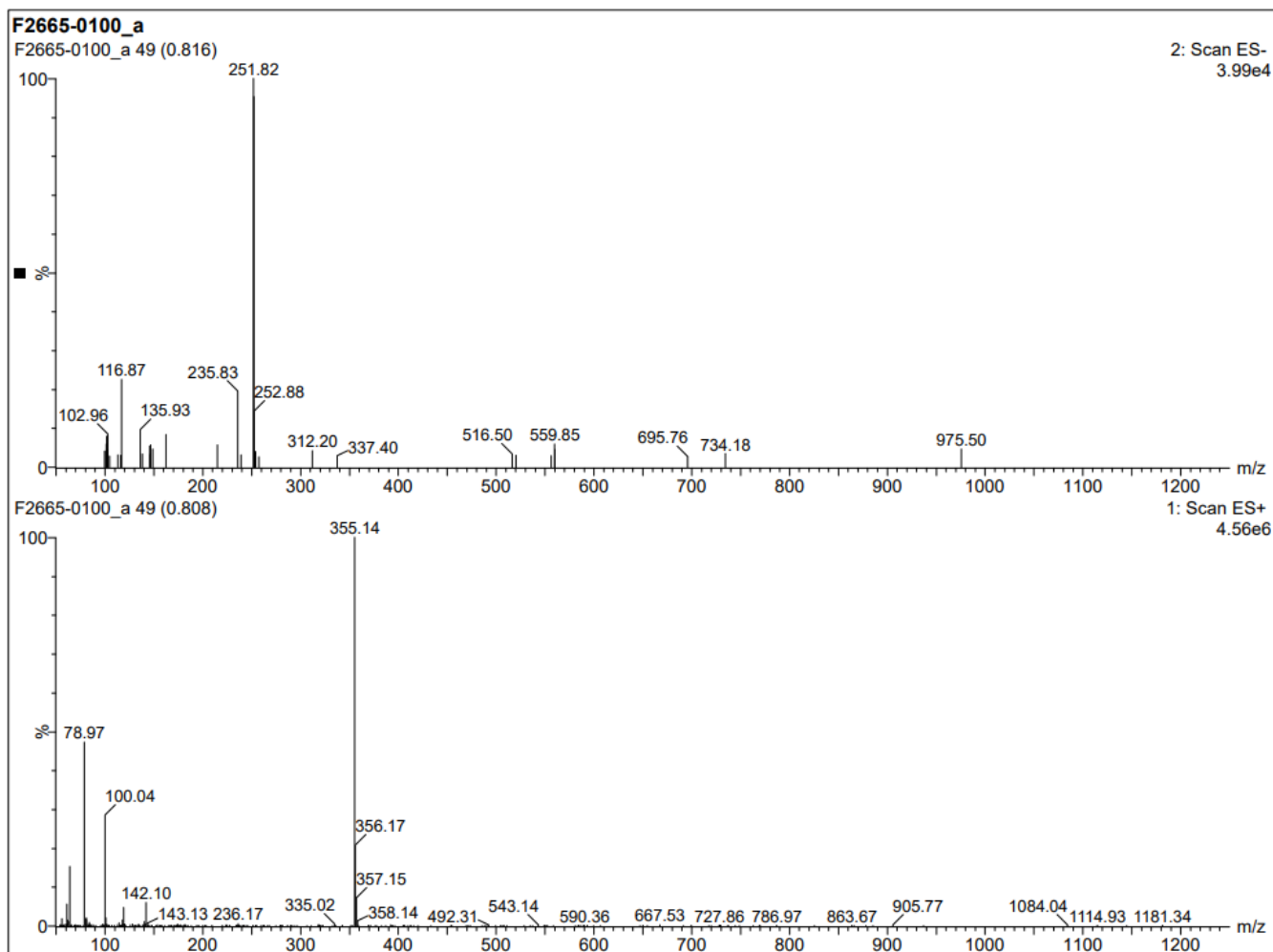
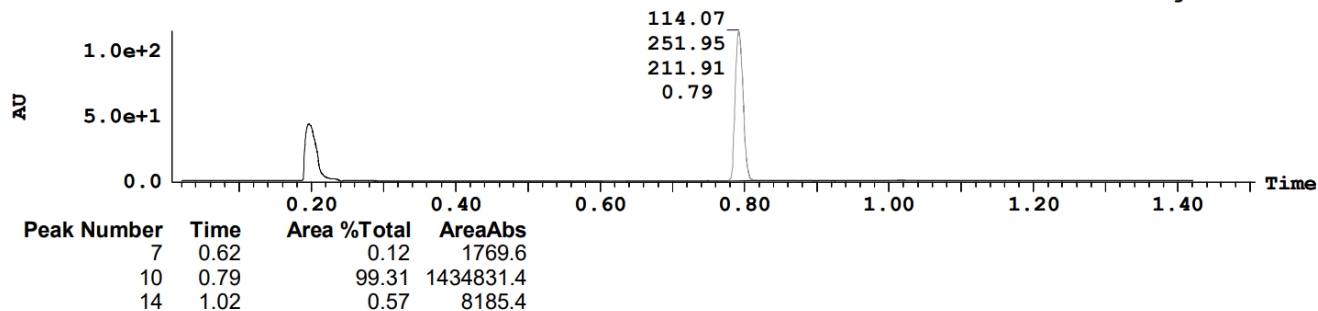
Peak Number	Time	Area %Total	AreaAbs
2	0.36	0.46	11290.9
3	0.39	0.36	8812.6
6	0.56	0.24	5846.8
8	0.66	1.03	25312.5
9	0.67	0.43	10558.7
10	0.69	0.32	7941.9
11	0.73	96.83	2372742.8
13	0.94	0.17	4125.9
14	0.98	0.15	3664.4



Supplementary Figure 6: LCMS purity of compound 5.

3: UV Detector: TAC: Wavelength Range: (210 - 350)

1.146e+2
Range: 1.149e+2



Supplementary Figure 7: LCMS purity of compound 7.

Isoform	Compound	GCI (waveRAPID®)			ITC					DSF
		K_D (nM)	k_a (M/s ⁻¹)	k_d (s ⁻¹)	K_D (nM)	ΔH (kcal.mol ⁻¹)	ΔG (kcal.mol ⁻¹)	$-T\Delta S$ (kcal.mol ⁻¹)	N	ΔT_m (°C)
BRPF1a	GSK6853	2.7×10^3	1.3×10^6	3.61	n.d.	n.d.	n.d.	n.d.	n.d.	+1.0
	NI-57	2.7×10^4	1.2×10^5	3.2	n.d.	n.d.	n.d.	n.d.	n.d.	+0.7
BRPF1b	GSK6853	7.8	1.3×10^6	1.0×10^{-2}	15	-16.2	-10.7	5.5	0.9	+19.9
	NI-57	8.6	1.9×10^7	1.6×10^{-1}	36	-7.4	-10.2	-2.7	1.3	+ 17

Supplementary Table 1: Comparison of **GSK6853** and **NI-57** binding to BRPF1a and BRPF1b.