

**Supporting Information for**

**Original article**

**Discovery of a potent and dual-selective bisubstrate inhibitor for protein arginine methyltransferase 4/5**

Ayad A. Al-Hamashi<sup>a,b</sup>, Dongxing Chen<sup>a</sup>, Youchao Deng<sup>a</sup>, Guangping Dong<sup>a</sup>, Rong Huang<sup>a,\*</sup>

<sup>a</sup>*Department of Medicinal Chemistry and Molecular Pharmacology, Center for Cancer*

*Research, Institute for Drug Discovery, Purdue University, West Lafayette IN 47907, USA*

<sup>b</sup>*Department of Pharmaceutical Chemistry, College of Pharmacy, University of Baghdad, Bab-almoadham, Baghdad 10047, Iraq*

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\*Corresponding author. Tel: +1 765 4943426.

E-mail address: [huang-r@purdue.edu](mailto:huang-r@purdue.edu) (Rong Huang).

## Table of contents

**Table S1** The single dose of HotSpot methyltransferases inhibition for a single dose (10  $\mu\text{mol/L}$ ) of AH237 on various methyltransferases. These data are associated with Fig. 3. 3

<b><math>^1\text{H}</math> NMR and <math>^{13}\text{C}</math> NMR Spectra</b> .....	4
<i>S</i> -(((3 <i>aS</i> ,4 <i>S</i> ,6 <i>R</i> ,6 <i>aR</i> )-6-(6-Amino-9 <i>H</i> -purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4- <i>d</i> ][1,3]dioxol-4-yl)methyl) ethanethioate ( <b>2</b> ) .....	4
2-(2-(((3 <i>aS</i> ,4 <i>S</i> ,6 <i>R</i> ,6 <i>aR</i> )-6-(6-Amino-9 <i>H</i> -purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4- <i>d</i> ][1,3]dioxol-4-yl)methyl)thio)ethyl)isoindoline-1,3-dione ( <b>4a</b> ) .....	5
2-(3-(((3 <i>aS</i> ,4 <i>S</i> ,6 <i>R</i> ,6 <i>aR</i> )-6-(6-Amino-9 <i>H</i> -purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4- <i>d</i> ][1,3]dioxol-4-yl)methyl)thio)propyl)isoindoline-1,3-dione ( <b>4b</b> ).....	5
<b>MALDI Spectra</b> .....	6
AH240 ( <b>1b</b> ) (Lys-C2-Ad). .....	6
AH244 ( <b>1f</b> ) (Lys-C3-Ad). .....	7
AH238 ( <b>1a</b> ) (Arg-C2-Ad). .....	8
AH246 ( <b>1e</b> ) (Arg-C3-Ad).....	9
AH218 ( <b>1d</b> ) (RGK-C2-Ad).....	10
AH221 ( <b>1h</b> ) (RGK-C3-Ad).....	11
AH233 ( <b>1c</b> ) (RGR-C2-Ad).....	12
AH237 ( <b>1g</b> ) (RGR-C3-Ad). .....	13

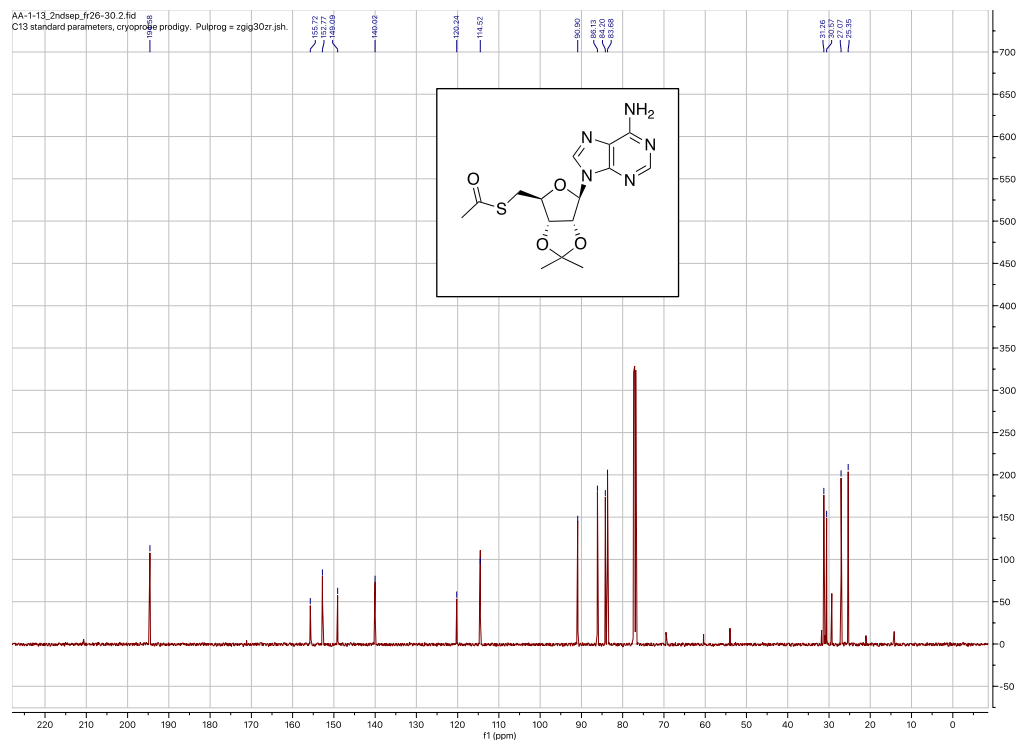
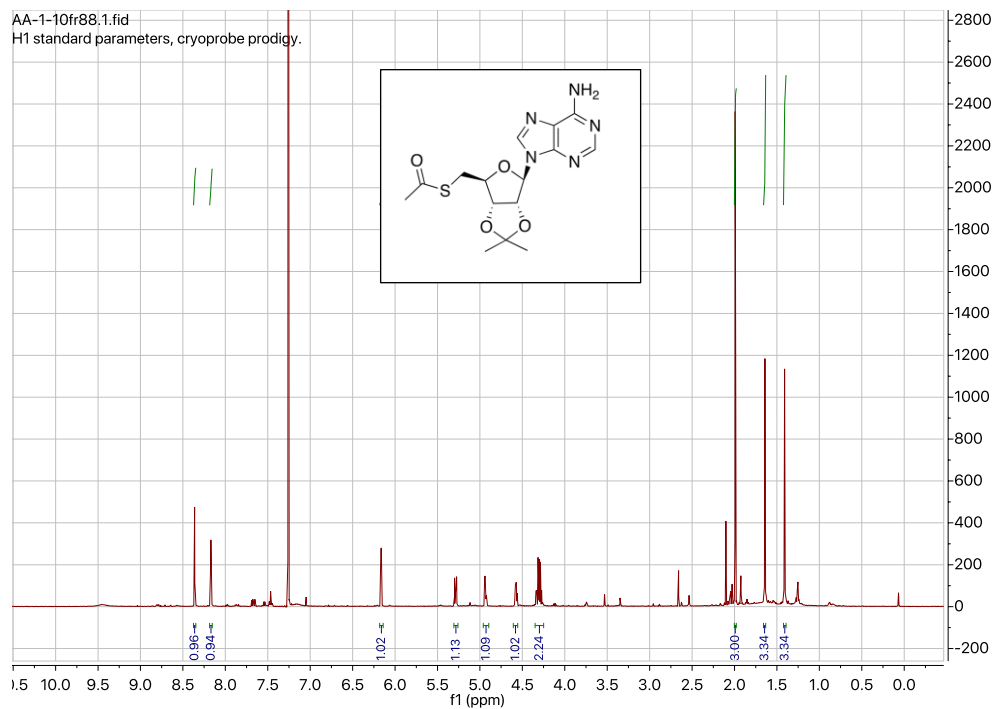
**Table S1** The single dose of HotSpot methyltransferases inhibition for a single dose (10  $\mu$ mol/L) of AH237 on various methyltransferases. These data are associated with Fig. 3.

Methyltransferase	% Enzyme activity*	Methyltransferase	% Enzyme activity*
ASH1L	100.10	NSD2 (E1099K)	107.95
DNMT1	94.27	NSD2 (T1150A)	108.71
DNMT3a	86.34	NSD3	102.65
DNMT3b	88.39	PRDM9	110.83
DNMT3b/3L	103.47	PRMT1	28.96
DOT1L	74.89	PRMT3	100.72
EZH1 Complex	92.13	PRMT4	0.28
EZH2 Complex	97.83	PRMT5/MEP50 Complex	0.20
EZH2(Y641F) Complex	95.23	PRMT5 (C449S)/MEP50 Complex	0.70
G9a	88.07	PRMT6	41.59
GLP	103.64	PRMT7	25.08
METTL21A	97.44	PRMT8	59.64
MLL1 Complex	111.76	SET1b Complex	96.84
MLL2 Complex	110.15	SET7/9	110.28
MLL3 Complex	102.61	SET8	99.68
MLL4 Complex	97.85	SETD2	91.70
NTMT1	102.22	SMYD2	50.67
NTMT2	91.14	SMYD3	50.28
NSD1	85.71	SUV39H1	100.32
NSD2	101.46	SUV39H2	100.12
		SUV420H1TV2	96.69

\*Relative to DMSO control.

# $^1\text{H}$ NMR and $^{13}\text{C}$ NMR spectra

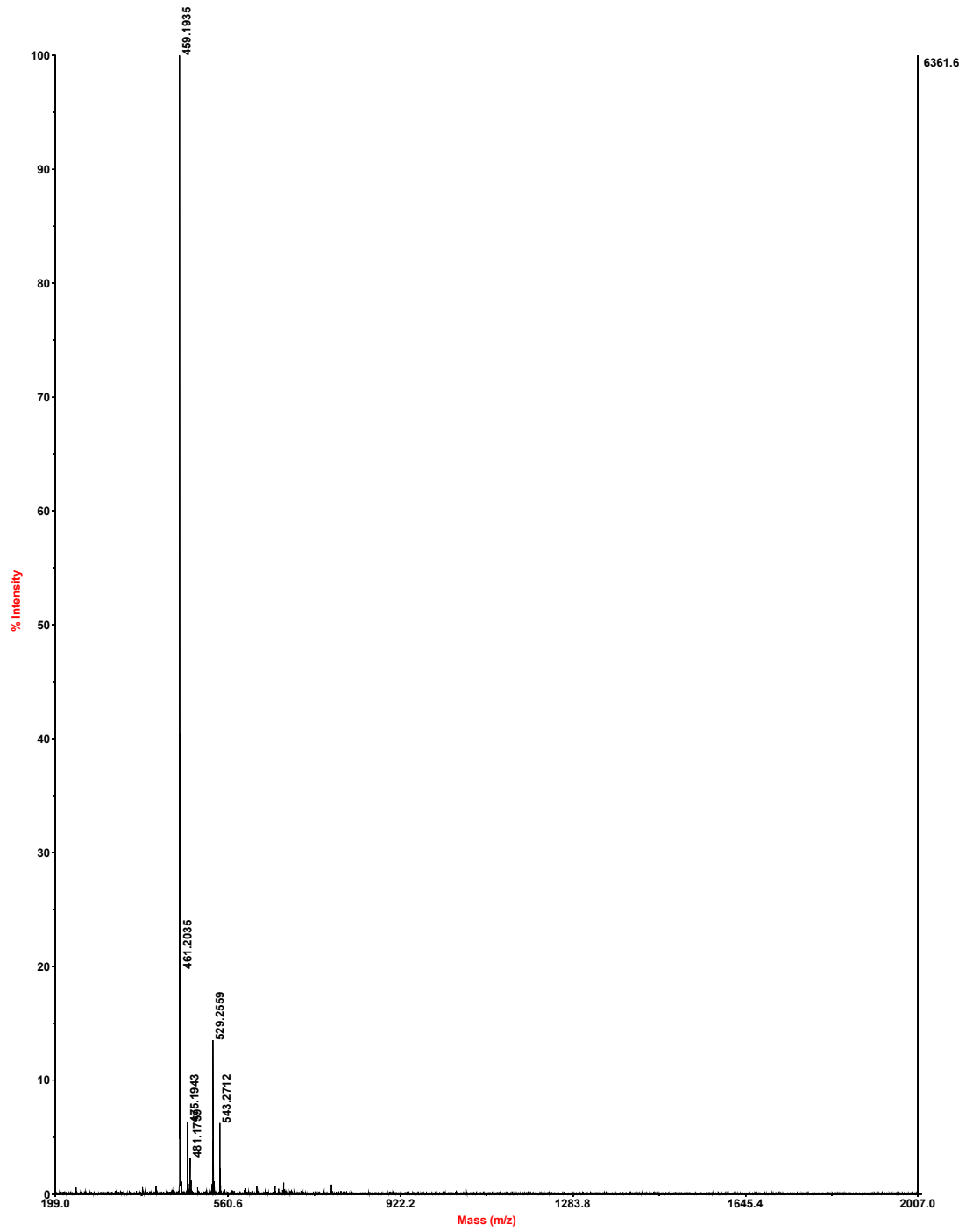
*S*-(((3*aS*,4*S*,6*R*,6*aR*)-6-(6-Amino-9*H*-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methyl) ethanethioate (**2**)



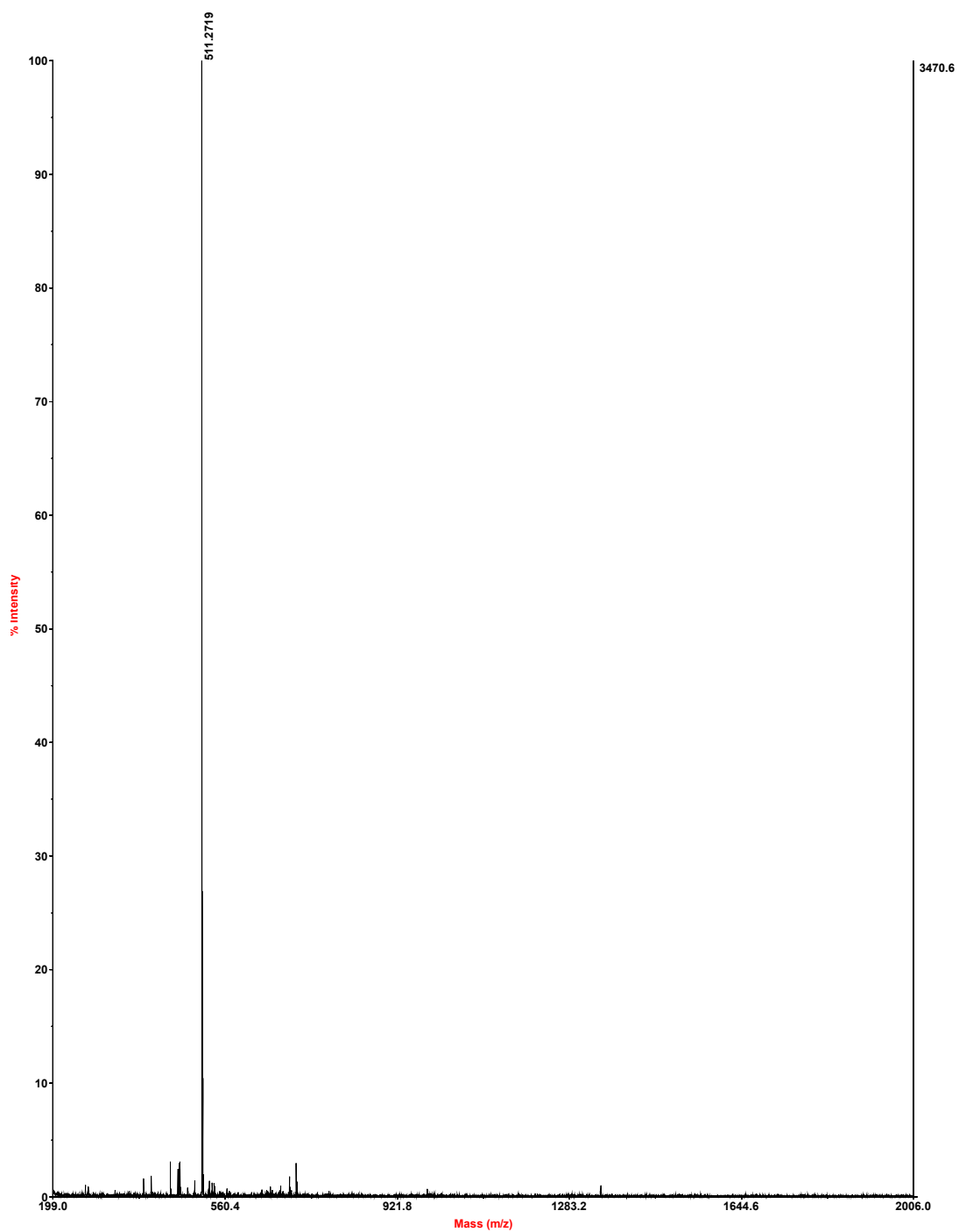


# MALDI spectra

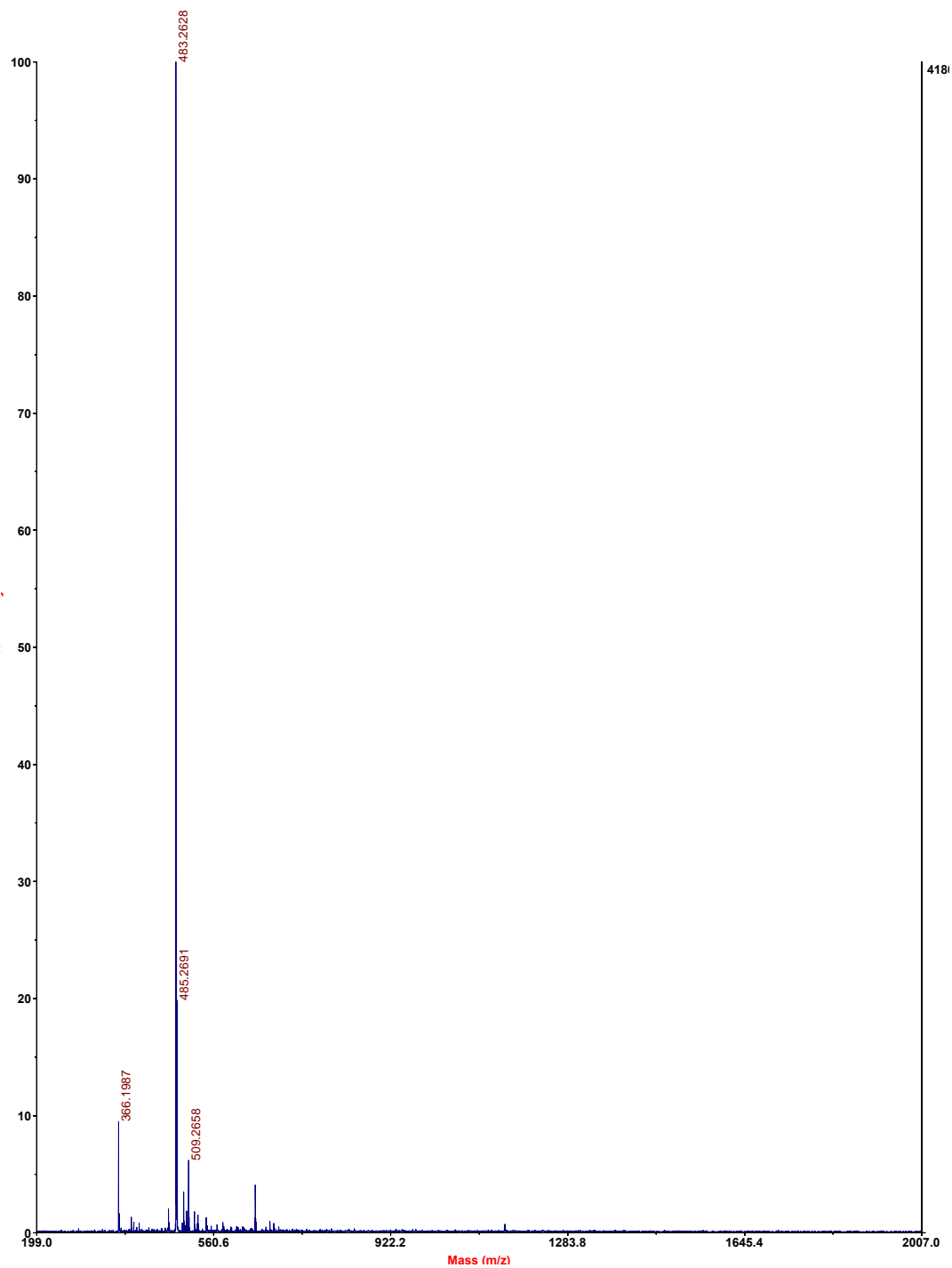
AH240 (1b) (Lys-C2-Ad).



AH244 (1f) (Lys-C3-Ad).

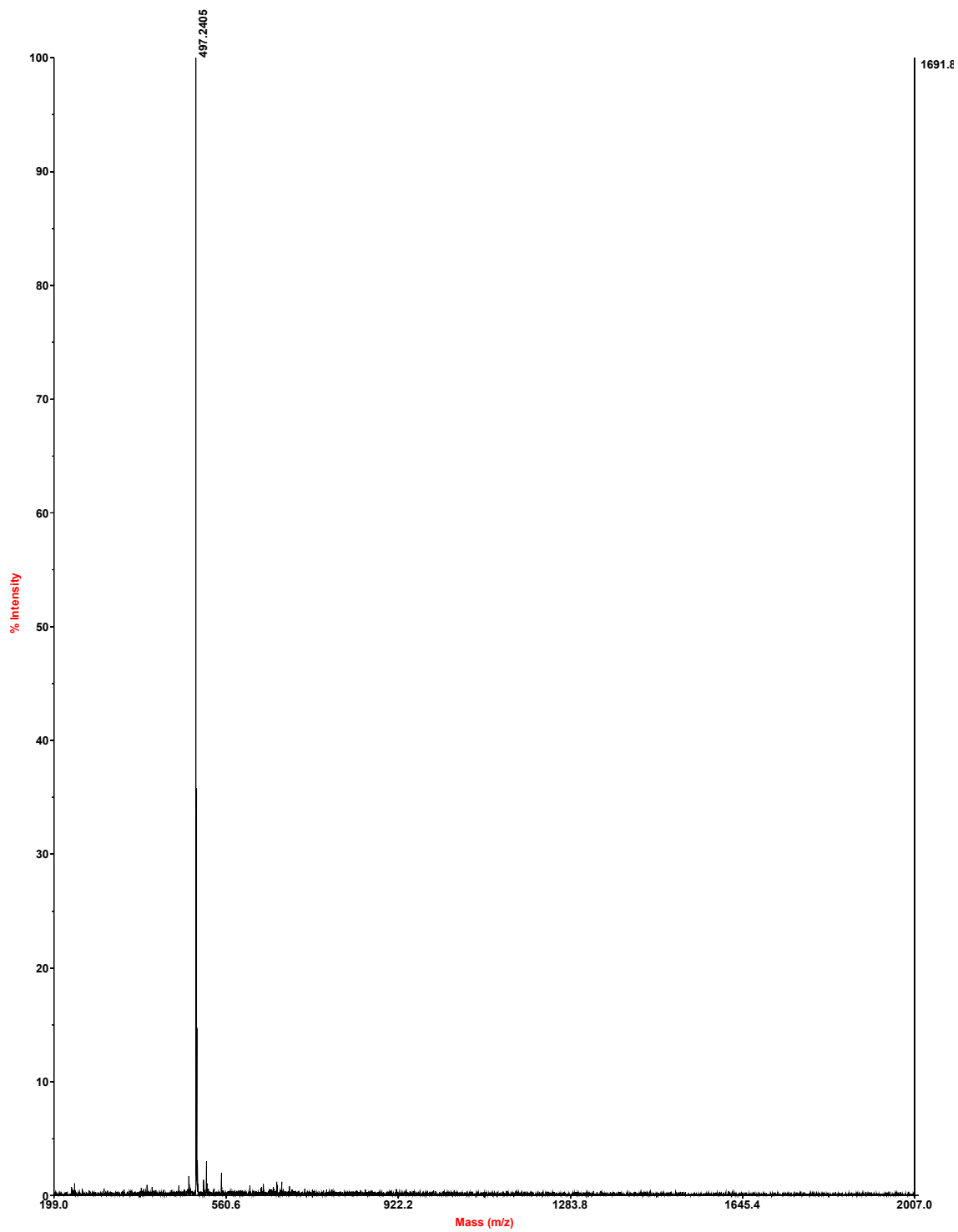


AH238 (1a) (Arg-C2-Ad).

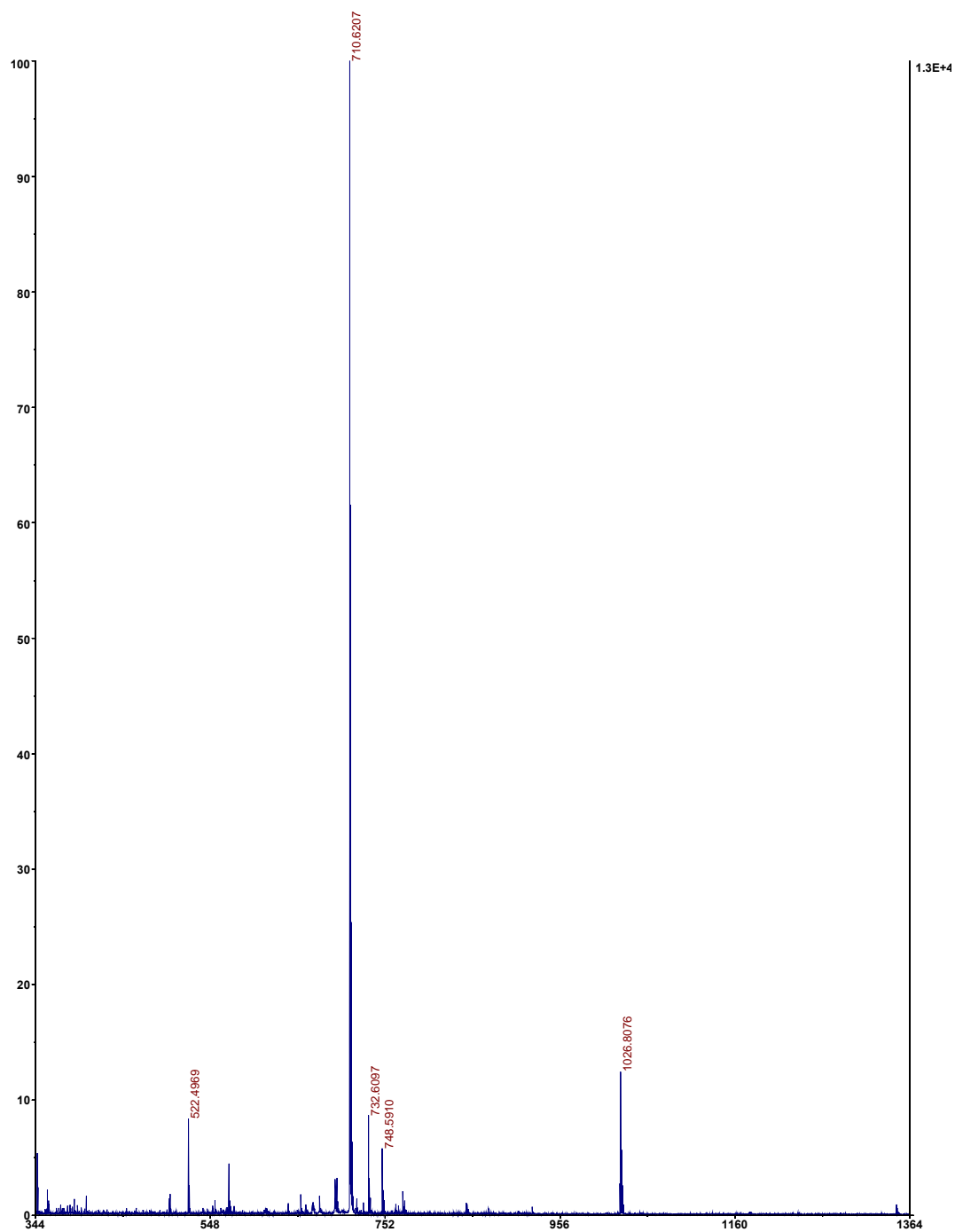




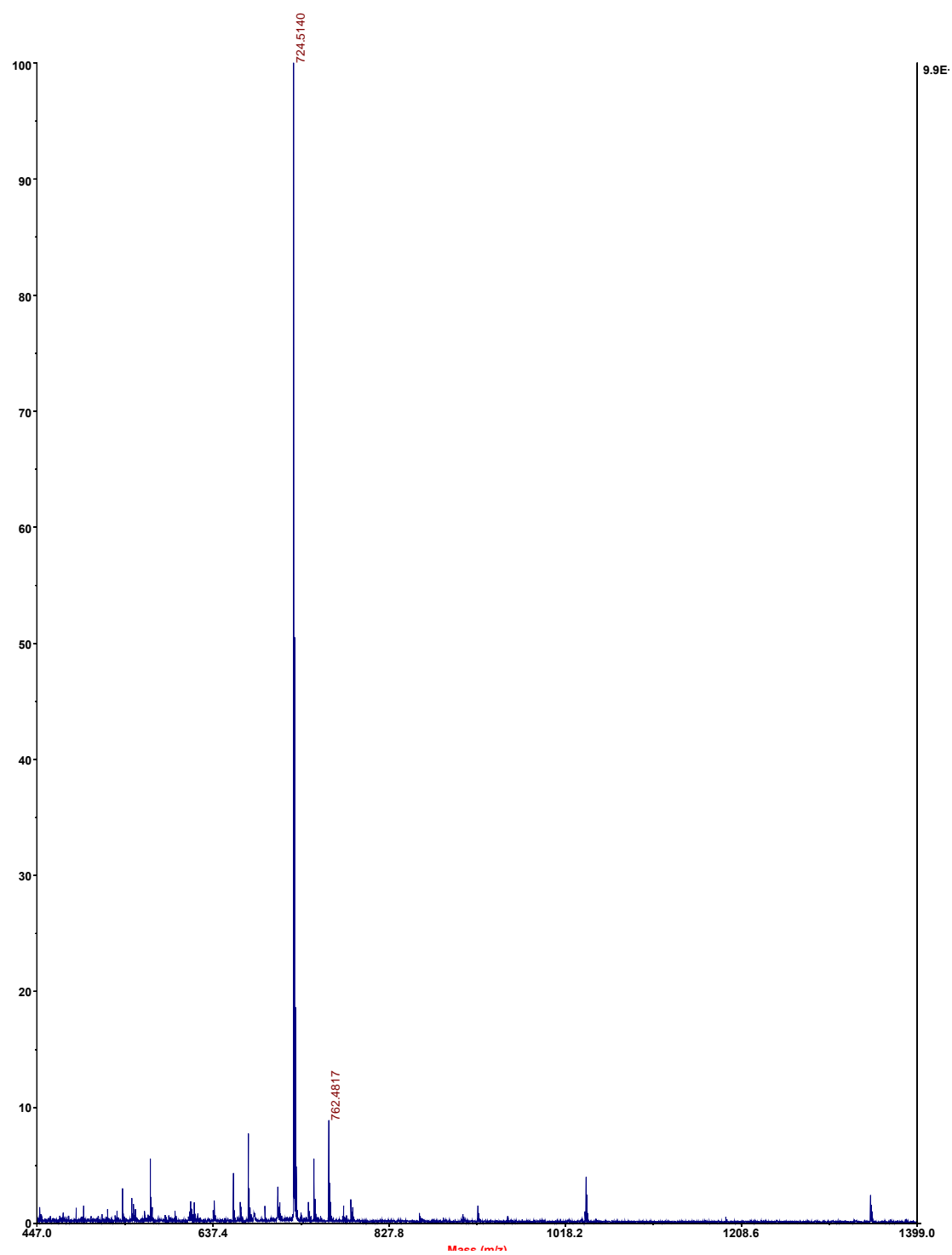
AH246 (1e) (Arg-C3-Ad).



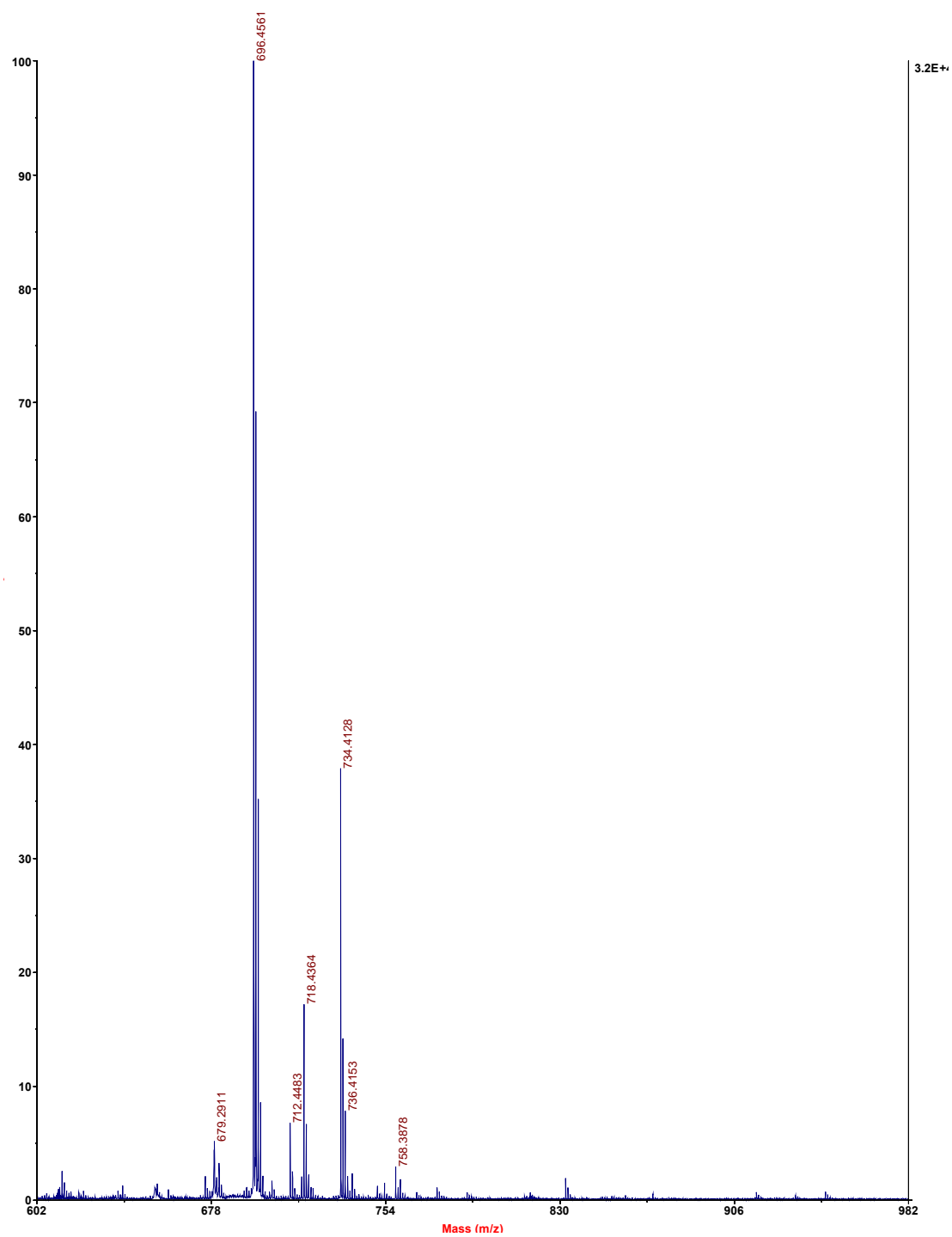
AH218 (1d) (RGK-C2-Ad).



AH221 (1h) (RGK-C3-Ad).



AH233 (1c) (RGR-C2-Ad).



AH237 (1g) (RGR-C3-Ad).

