## SUPPORTING INFORMATION FOR: Inhibitor Binding of Group IVA Phospholipase A<sub>2</sub> Probed by Molecular Dynamics and Deuterium Exchange Mass Spectrometry

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Supplemental Figure 1 Deuterium exchange upon binding of 10  $\mu$ M pyrrophenone or AX007. The number of incorporated deuterons at seven time points are displayed in peptides that overlap peptides displayed in Figures 3 and 5. Peptides 240-253, and 379-393 are given as examples of peptides with no change in exchange upon inhibitor binding.



Supplemental Figure 2 Modeling uncrystalized residues in  $PLA_2$ . The residues without defined electron density in the crystallographic structure were modeled and are shown in purple.

## GIVA PLA<sub>2</sub> Protein Digest Map

1	10	20	30	40	50	60	70	80	90	100
MSFIDP	<u>(OHIIVEHQY</u>	SHKFTVVVLR	ATKVTKGAFO	DMLDTPDPYV	ELFISTTPDS	RKRTRHFN N	DINPVWNETFE	FILDPNOENV	LEITLMDANY	VMDE
								▝▕▌▋▌▌▌▌	II.	
101	110	120	130	140	150	160	170	180	190	200
TLGTATI	TVSSMKVGE	KKEVPFIFNÇ	VTEMVLEMSI	EVCSCPDLRF	SMALCDQEKI	FRQQRKEH I	RESMKKLLGPK	NSEGLHSARD	VPVVAILGSG	GGFR
201	210	220	230	240	250	260	270	280	290	300
AMVGFS0	GVMKALYESG	ILDCATYVAG	LSGSTWYMSI	LYSHPDFPEK	GPEEINEELM	IKNVSHNPL L	LLTPQKVKRYV	ESLWKKKSSC	<u>OPVTFTDIFG</u>	MLIG
								11111		
301	310	320	330	340	350	360	370	380	390	400
ETLIHN	RMNTTLSSLK	EKVNTAQCPL	PLFTCLHVKF	DVSELMFADW	VEFSPYEIGM	IAKYGTEMA P	DLFGSKFFMGT	VVKKYEENPL	HF LMG VWG SA	FSIL
										=
401	410	420	430	440	450	460	470	480	490	500
FNRVLG	/SGSQSRGSI	MEEELENIII	KHIV SND SSL	JSDDESHEPKG	TENEDAGSDI	QSDNQASW I	HRMIMALVSDS	ALFNIREGRA	GK VHNFMLGL	N LN I
5.01	510	500	500	E 40		5.60	570	500	500	600
SYPLSPI	SDFATODSF	JZU DDDELDAAVA	DPDEFERTYF	DVKSKKTH	550 VVDSGLTENI	.PYPLTLRP O	BGVDLTTSFDF	SARPSDSSPF	FKELLLAEKW	A KMN
o ir bor										
601	610	620	630	640	650	660	670	680	690	700
KLPFPK	LDPYVFDREG	LKECYVFKPK	NPDMEKDCP1	TIHFVLANIN	FRKYKAPGVE	RETEEEKE I	ADFDIFDDPES	PFSTFNFQYF	NQAFKRLHDL	MHFN
			<u></u>	<u></u>				<u></u>	<u></u>	¥
									,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	<b>IIII</b>
701	710	720	730	740	749					
TLNNID	/IKEAMVESI	EYRRQNPSRC	SVSLSNVEAF	REFNKEFLSK	РКА					
			- <u></u>							

**Supplemental Figure 3 Peptide digest map of GIVA PLA<sub>2</sub>.** Identified and analyzed peptides resulting from pepsin-digestion are shown below the primary sequence of GIVA PLA<sub>2</sub>. All peptides were analyzed, but to prevent redundancy only the peptides shown as solid lines were used in this study.



Supplemental Figure 4 Root mean square distance of protein and inhibitor. For all  $C_{\alpha}$  RMSD measurements the red represents the RMSD of all residues, with crystallized residues RMSD shown in blue (excluding 407-414, 431-462, 498-538, and 626-632). a) The RMSD of the  $C_{\alpha}$  in the apoenzyme over the simulation time course (50 ns). b) The RMSD of the  $C_{\alpha}$  in the pyrrophenone bound enzyme. c) The RMSD of the  $C_{\alpha}$  in the oxoamide bound enzyme. d) The RMSD values of both the oxoamide (green) and pyrrophenone (red) over the simulation time course is plotted.



**Supplemental Figure 5 Regions in contact with inhibitors with extremely fast or slow rates of exchange.** Region 403-417 (A) and 294-298 (B) are plotted showing extremely fast rates of exchange (region 403-417), or extremely slow rates (region 294-298), with or without pyrrophenone or oxoamide present.