

CORPUS PHARMS										Stability protocol for Xanomeline / Trospium HCl Pellets										Manufacturing date: 2016DE12, Incubation date: 2016DE16									
Project	Lot (Strength)	Packaging	Stability conditions			Time points (month)																							
			25°C/ 60% RH	30°C/ 65% RH	40°C/ 75% RH	0	1	2	3	6	EXTRA																		
286-02	OT20 Xanomeline 50mg (fb) Trospium HCl 20mg	30cc HDPE bottles with sealed PP cap	6 bottles (20 capsules/bottle)			2016DE16	2017JA16	2017FE16	2017MR16	2017JN16	TBD																		
				6 bottles (20 capsules/bottle)			2017JA16	2017FE16	2017MR16	2017JN16	TBD																		
					4 bottles (20 capsules/bottle)		2017JA16	2017FE16	2017MR16	2017JN16	TBD																		
	OT20 Xanomeline 50mg (fb) Trospium HCl 10mg		5 bottles (20 capsules/bottle)				2017JA16	2017FE16	2017MR16	2017JN16	TBD																		
				6 bottles (20 capsules/bottle)			2017JA16	2017FE16	2017MR16	2017JN16	TBD																		
					3 bottles (20 capsules/bottle)		2017JA16	2017FE16	2017MR16	2017JN16	TBD																		
Sample to be analyzed for:																													
Appearance, Assay, Related Substances, KF and Dissolution																													
At the Client request, sample will be removed from chamber and analyzed.																													

FIG 1

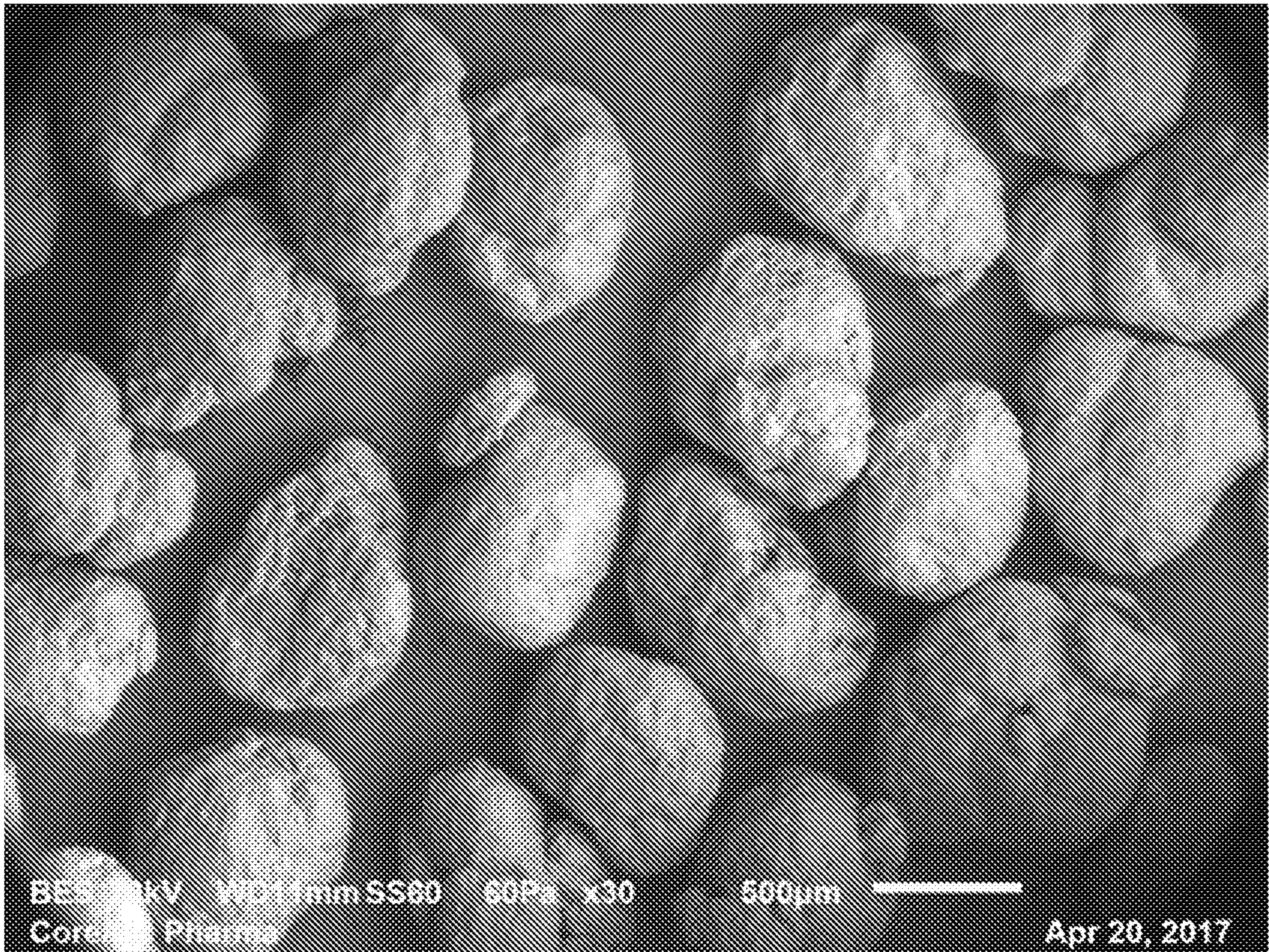


FIG 2

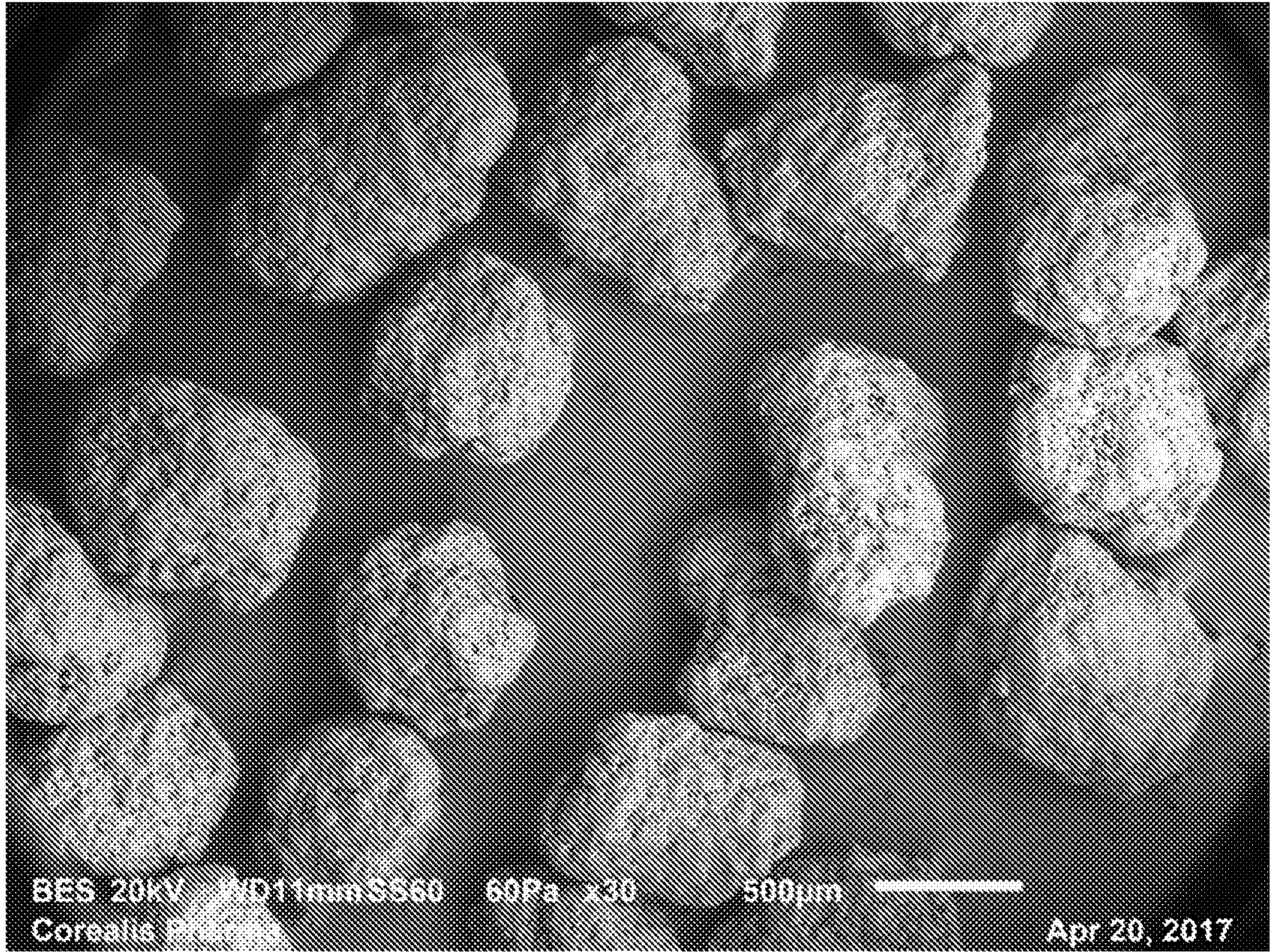


FIG. 3

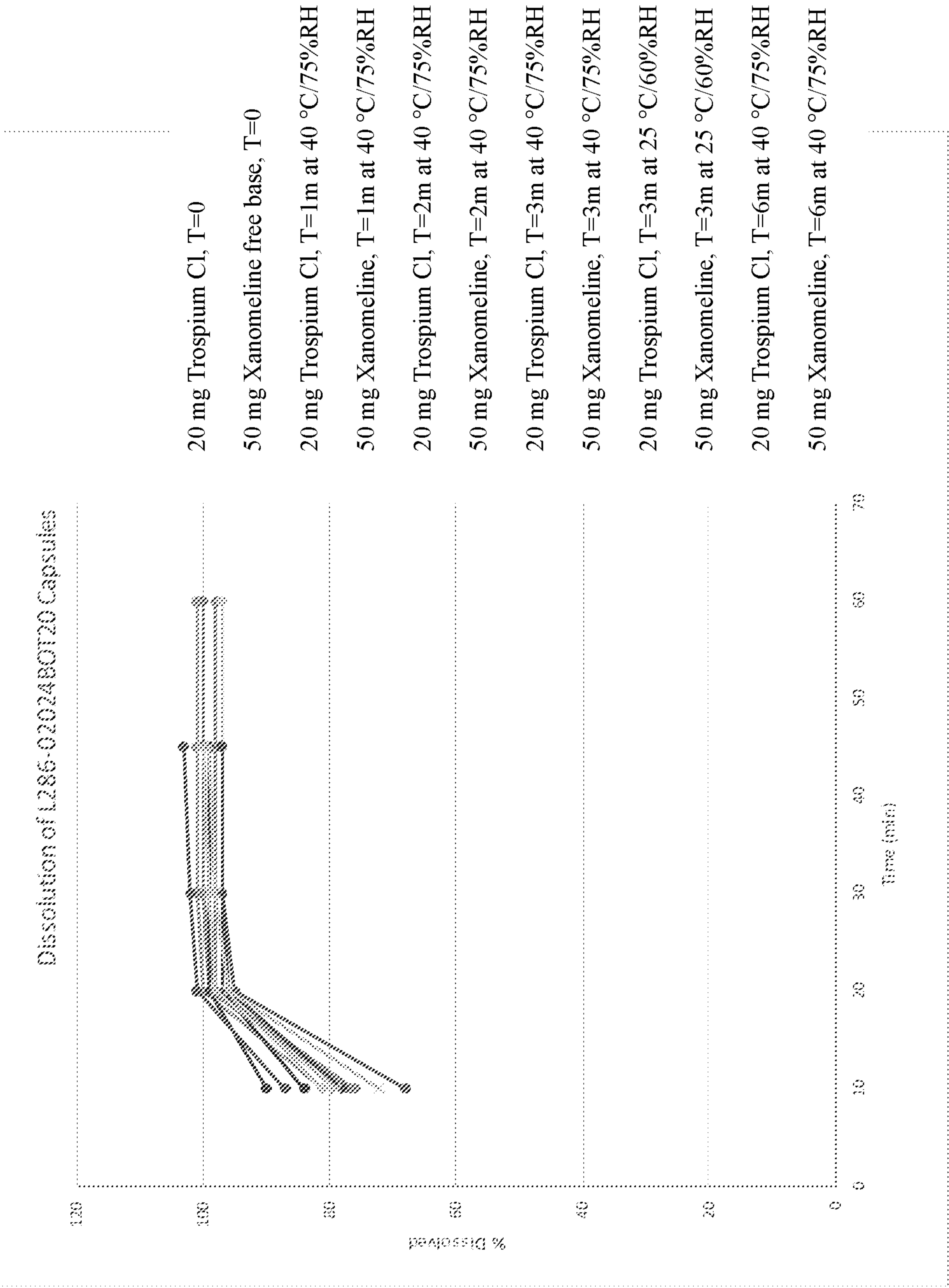


FIG. 4

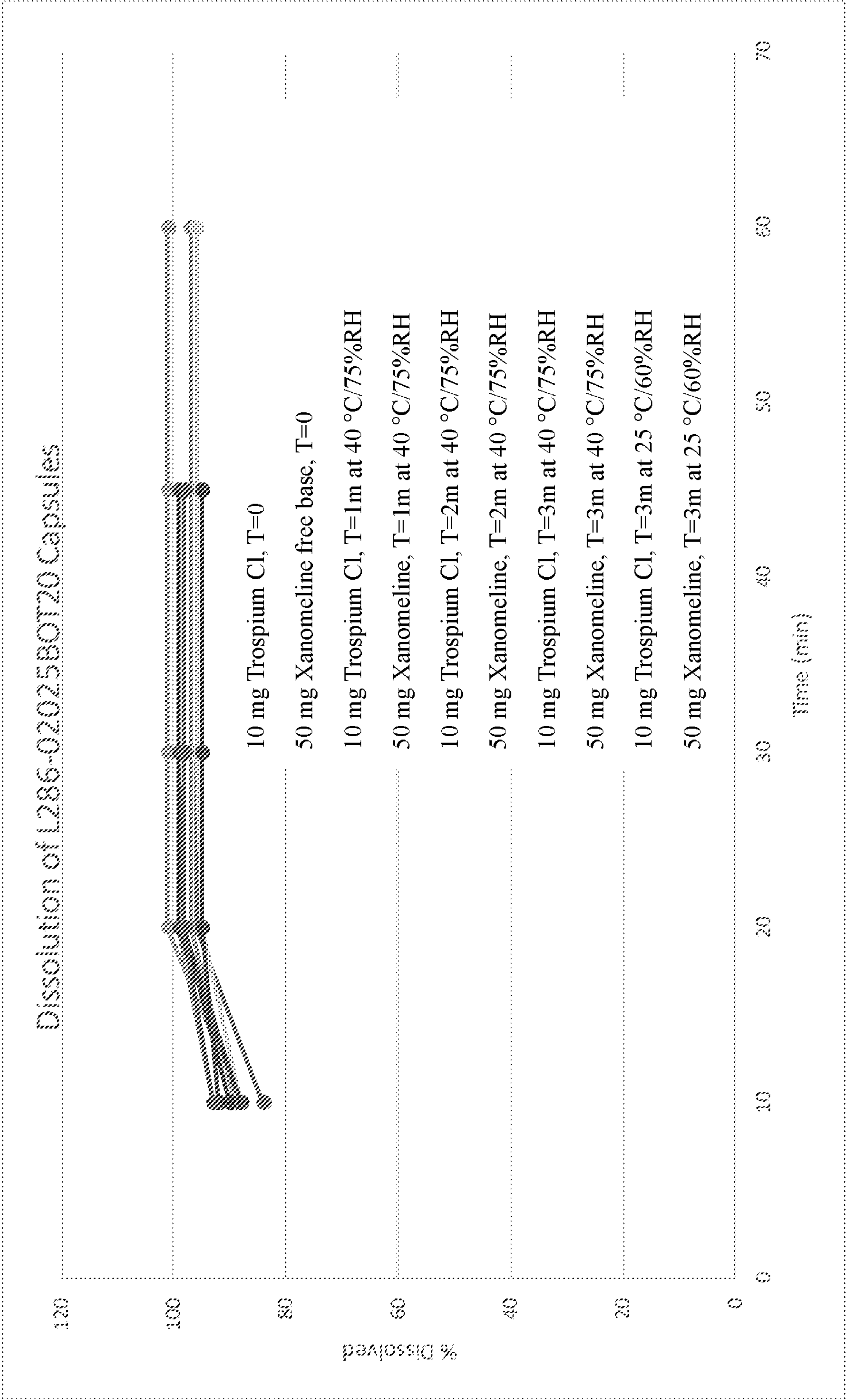


FIG. 5

STORAGE		25°C/60%RH	
TEST DESCRIPTION		3 Months	6 Months
SPECIFICATION used at time of analysis		Stability, Rev 01	Stability, Rev 01
Conforms to acceptance criteria (Y/N) Description (Rev 01) Water content by KF (USP <921>, Method 1a) (n=3)		Y	Y
		No change as compared to initial	No change as compared to initial
		2.6	2.5
Assay (Concise-28502-AD-01) (n=2)	% label claim Xanoxamine	104.5 ^a	102.3
	mg Xanoxamine/capsule	52.3 ^a	51.2
	% label claim Trosipium Chloride	97.5 ^c	97.8
	mg Trosipium Chloride/capsule	9.8 ^c	9.8
	Method Revision	01	02
Related substances (%LC) ^{a,b} (Concise-28502-AD-01) (n=2)	Trosipium Chloride related compound B	Not detected ^a	Not detected
	Trosipium Chloride related compound A	Not detected ^a	Not detected
	Unspecified impurity (Xanoxamine, PRT10.23) ^{a,c}	0.14	0.14
	Unspecified impurity (Xanoxamine, PRT11.06) ^{a,c}	0.18	0.16
	Total Impurities	0.32 ^a	0.30
	Method Revision	01	02

FIG. 6

STORAGE		30°C/65%RH	
TEST DESCRIPTION		3 Months	
SPECIFICATION used at time of analysis		Stability, Rev 01	
		Stability, Rev 01	
Conforms to acceptance criteria (V74)		0	
Description		Y	
(Visual)		Y	
Water content by KF		No change	
(USP <921>, Method 1a)		as compared to initial	
(n=3)		2.5	
Assay		2.7	
(Coreals-28502-AD-01)		102.3	
(n=2)		51.2	
Related substances		98.4	
(NLC) ^A		9.8	
(Coreals-28502-AD-01)		0.14	
(n=2)		0.18	
Total impurities		0.30	
Method Revision		01	
Trospium Chloride related compound B		Not detected	
Trospium Chloride related compound A		Not detected	
Unspecified impurity		Not detected	
(Xanomeline, PFT0.24) %		0.14	
Unspecified impurity		0.18	
(Xanomeline, PFT1.03) %		0.30	
Total impurities		0.30	
Method Revision		01	

FIG. 7

STORAGE		T=0		45°C/75%RH	
TEST DESCRIPTION		3 Months		6 Months	
SPECIFICATION used at time of analysis		Stability, Rev 01		Stability, Rev 01	
Conforms to acceptance criteria (Y/N)		Y		Y	
Description (Value)		OT-white opaque hard shell capsule with no markings		No change as compared to initial	
Water content by KF (USP <821>, Method 1a) (n=3)	%water	2.4		2.5	
	% label claim Xanomeline	104.5 %		99.8	
	mg Xanomeline/capsule	82.3 %		83.6	
	% label claim Trospium Chloride	97.5 %		97.0	
	mg Trospium Chloride/capsule	9.8 %		9.7	
Assay (Compass-28502-AD-01) (n=2)		Method Revision		01	
Related substances (%LC) ^a (Compass-28502-AD-01) (n=2)	Trospium Chloride related compound B	Not detected ^c		Not detected	
	Trospium Chloride related compound A	Not detected ^c		Not detected	
	Unspecified Impurity (Xanomeline, NRT024) ^{a, b}	0.15 %		0.14	
	Unspecified Impurity (Xanomeline, NRT103) ^{a, b}	-		0.14	
	Total impurities	0.15 %		0.28	
Method Revision		0		01	

FIG. 8

STORAGE		Y=Q		25°C/60%RH		3 Months		6 Months		9 Months	
TEST DESCRIPTION		Release, Rev 0		Stability, Rev 01		Stability, Rev 01		Stability, Rev 01		Stability, Rev 01	
SPECIFICATION used at time of analysis		Release, Rev 0		Stability, Rev 01		Stability, Rev 01		Stability, Rev 01		Stability, Rev 01	
Confirms to acceptance criteria (Y/N)		Y		Y		Y		Y		Y	
Dissolution (NLT) (Covers 25002-B-01) (n=6) (2500 mL of 0.1N HCl, rotate at 50 rpm)		Kanamycin Time (min.)	%LC	Range	%LC	Range	%LC ^a	Range ^b	%LC	Range	%LC
		10	54	12-58	30	7-67	34	1-74	47	28-62	47
		20	98	90-102	95	75-97	98	82-101	98	95-102	98
		(Q=95%) 30	100	102-104	100	98-101	99	87-102	101	98-103	101
		45	103	103-104	102	101-103	102	98-103	101	101-102	101
		Tropium Chloride Time (min.)	%LC	Range	%LC	Range	%LC ^a	Range ^b	%LC	Range	%LC
		10	49	11-53	27	6-60	32	0-65	43	23-63	43
		20	88	67-98	88	72-99	93	56-97	95	88-100	95
		(Q=95%) 30	95	94-102	97	92-103	95	81-100	98	94-104	98
		45	96	94-102	99	95-103	97	90-104	99	95-104	99
		Method Revision		0		01		01		01	
		Total Yeasts and Molds Counts (TYMCL) x100 cfu/g		<50 cfu/g		N/A		N/A		N/A	
		Total Aerobic Microbial Counts (TAMC) x1000 cfu/g		< 500 cfu/g		N/A		N/A		N/A	
		Enterobacteriaceae Count		Absent		N/A		N/A		N/A	

FIG. 9

STORAGE		Y=0		3 Months		6 Months	
TEST DESCRIPTION		Release, Rev 0		Stability, Rev 01		Stability, Rev 01	
SPECIFICATION used at time of analysis		7-0138					
Conforms to acceptance criteria (Y/N)							
Dissolution (%L.C) (Conc'd-20002-0-01) (n=6) (500 mL of 0.1N HCl, particles at 50 rpm)	Xenomeltine Time (min)	%L.C	Range	%L.C	Range	%L.C	Range
	10	54	12-89	35	14-58	35	3-54
	20	88	80-102	85	80-98	97	88-103
	(Q=80%) 30	103	102-104	101	99-103	102	100-104
	45	103	103-104	102	103-104	103	101-104
	Prospan Chloride Time (min)	%L.C	Range	%L.C	Range	%L.C	Range
	10	49	11-83	30	9-34	20	2-56
	20	93	87-98	84	69-93	92	81-100
	(Q=80%) 30	96	94-102	96	94-102	97	93-105
	45	96	94-102	99	95-102	97	93-105
Method Revision:		0		01		01	
Total Yeasts and Molds Counts (TYMC) ≤100 cfu/g		≤50 cfu/g		N/A		N/A	
Total Aerobic Microbial Counts (TAMC) ≤1000 cfu/g		≤ 500 cfu/g		N/A		N/A	
Escherichia coli: Absent		Absent		N/A		N/A	
Microbial Limits * USP <61>, <62>							

FIG. 10

STORAGE		T = 0		40°C/75%RH	
TEST DESCRIPTION		3 Months		8 Months	
SPECIFICATION used at time of analysis		Release, Rev 0		Stability, Rev 01	
Conforms to acceptance criteria (Y/N)		Y		Y	
Dissolution (%L.C) (Conc=20002-0-01) (n=6) (200 mL of 0.1N HCl, rotates at 50rpm)	Xanthenine Time (min)	%L.C	Range	%L.C	Range
	10	94	12-89	45	6-90
	20	98	90-102	89	80-99
	(Q=80%) 30	103	102-104	98	93-101
	45	103	103-104	100	98-101
	Tropium Chloride Time (min)	%L.C	Range	%L.C	Range
	10	49	11-63	42	3-85
	20	93	87-98	86	74-94
	(Q=80%) 30	98	94-102	85	87-101
	45	98	94-102	97	92-103
Method Revision		0		01	
Microbial Limits* (USP<61>, <62>)	Total Yeasts and Molds Counts (TYMCO) ≤100 cfu/g	<50 cfu/g		N/A	
	Total Aerobic Microbial Counts (TAMCO) ≤1000 cfu/g	< 500 cfu/g		N/A	
	Escherichia coli: Absent	Absent		N/A	

FIG. 11

Xanomeline API Related Substances Profile for Xanomeline/Trospium Cl 50/10 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months	T= 9 months
Related Substances (%w/w) (n=1) (Corealis-28602-AD-01)	Unspecified impurity (PRT 0.23)	0.14	0.14	0.14	0.14
	Unspecified impurity (PRT 1.09)	<0.1	0.16	0.14	0.18
	Method Revision	0	01	02	03

FIG. 12

Trospium Chloride API Related Substances Profile for Xanomeline/Trospium Cl 50/10 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months	T= 9 months
Related Substances (%w/w) (n=1) (Corealis-28602-AD-01)	Unspecified impurity	Not Detected	Not Detected	Not Detected	Not Detected
	Method Revision	0	01	02	03

FIG. 13

Specification for Xanomeline/Trospium Cl 50/10 mg Capsules

TEST DESCRIPTION	ACCEPTANCE CRITERIA	ACCEPTANCE CRITERIA
	Release, Rev 0	Stability, Rev 01
Description (Visual)	White to off-white opaque hard shell capsule with no markings	White to off-white opaque hard shell capsule with no markings
Water Content by KF (USP <921>, Method 1a)	Report result	Report results
Assay (%LC) (Corealis-28602-AD)	Xanomeline: 90 - 110% label claim (45 - 55 mg Xanomeline/capsule)	Xanomeline: 90 - 110% label claim (45 - 55 mg Xanomeline/capsule)
	Trospium Chloride: 90 - 110% label claim (9 - 11mg Trospium Chloride/capsule)	Trospium Chloride: 90 - 110% label claim (9 - 11mg Trospium Chloride/capsule)
Related Substances (%LC) ^A (Corealis-28602-AD)	Trospium Chloride related compound B: NMT 0.2%LC	Trospium Chloride related compound B: NMT 0.2%LC
	Trospium Chloride related compound A: NMT 0.2%LC	Trospium Chloride related compound A: NMT 0.2%LC
	Any single unspecified impurity: NMT 0.2%LC	Any single unspecified impurity: NMT 0.2%LC
	Total Impurities: NMT 1.5%LC	Total Impurities: NMT 1.5%LC
Dissolution (Corealis-28602-B)	Xanomeline: NLT 80% (Q) of labeled amount of Xanomeline is dissolved at 30 minutes. Report profile	Xanomeline: NLT 80% (Q) of labeled amount of Xanomeline is dissolved at 30 minutes. Report profile
	Trospium Chloride: NLT 80% (Q) of labeled amount of Trospium Chloride is dissolved at 30 minutes. Report profile	Trospium Chloride: NLT 80% (Q) of labeled amount of Trospium Chloride is dissolved at 30 minutes. Report profile
Microbial Limits ^B USP<61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g
	Escherichia coli: Absent	Escherichia coli: Absent

FIG. 14

STORAGE		T=0		25°C/60%RH	
TEST DESCRIPTION		3 months		6 months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y	
Description (Y/N)		Y		Y	
Water content by KF (USP <921>, Method 1a) (n=3)		2.9		2.7	
Assay (Concals-28802-AD-01) (n=2)	% label claim Xanomeline	101.9		101.9	
	mg Xanomeline/capsule	50.9		51.0	
	% label claim Trospium Chloride	98.3		98.2	
	mg Trospium Chloride/capsule	19.7		19.6	
	Method Revision	01		02	
Related substances (%LC) ^A (Concals-28802-AD-01) (n=2)	Trospium Chloride related compound B	Not detected		Not detected	
	Trospium Chloride related compound A	Not detected		Not detected	
	Unspecified impurity (Xanomeline, RRT0.23) c.b	0.13		0.14	
	Unspecified impurity (Xanomeline, RRT1.05) c.b	0.17		0.14	
	Total Impurities	0.30		0.28	
Method Revision		01		02	

FIG. 15

STORAGE		30°C/65%RH	
TEST DESCRIPTION		T=0	
SPECIFICATION used at time of analysis		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y	
Description (Visual)		Off-white opaque hard shell capsule with no markings	
Water content by KF (USP <921>, Method 1a) (n=3)		%w/w 2.9	
Assay (Compass-28802-AD-01) (n=2)	% label claim Xanomeline	101.8	
	mg Xanomeline/capsule	50.9	
	% label claim Trospium Chloride	98.3	
	mg Trospium Chloride/capsule	19.7	
	Method Revision	01	
Related substances (%LC) ^a (Compass-28802-AD-01) (n=2)	Trospium Chloride related compound B	Not detected	
	Trospium Chloride related compound A	Not detected	
	Unspecified impurity (Xanomeline_PRT0.23) c, b	0.13	
	Unspecified impurity (Xanomeline_PRT1.03) c, b	0.17	
	Total Impurities	0.30	
	Method Revision	01	
		03	
		No change as compared to initial	
		8 months	
		Stability, Rev 0	

FIG. 16

STORAGE		40°C/75%RH	
TEST DESCRIPTION		3 months	
SPECIFICATION used at time of analysis		6 months	
		Stability, Rev 0	Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y	N
Description (Visual)		No change as compared to initials	
Water content by KF (USP <921>, Method 1a) (n=3)	%w/w	2.9	3.1
Assay (Corealis-28502-AD-01) (n=2)	% label claim Xanomeline	101.8	100.9
	mg Xanomeline/capsule	50.9	50.5
	% label claim Trospium Chloride	98.3	96.2
	mg Trospium Chloride/capsule	19.7	19.2
	Method Revision	01	03
Related substances (%LC) ^a (Corealis-28502-AD-01) (n=2)	Trospium Chloride related compound B	Not detected	Not detected
	Trospium Chloride related compound A	Not detected	0.14
	Unspecified impurity (Xanomeline_RPT0.23) c, b	0.13	0.14
	Unspecified impurity (Xanomeline_RPT1.08) c, b	0.17	0.28 ^b
	Total impurities	0.30	0.54
	Method Revision	01	03

FIG. 17

STORAGE		T=0		25°C/60%RH	
TEST DESCRIPTION				3 months	6 months
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y		Y	Y
Dissolution (%LC) (Comstat-28802-B-01) (n=6) (300 mL of 0.1N HCl packets at 50 rpm)	Xanomeline				
	Time (min.)				
	10	34	0-68	27	11-46
	20	89	64-97	94	85-101
	(Q=80%) 30	100	88-105	102	99-105
	45	103	99-106	103	99-105
	Tropium Chloride				
	Time (min.)				
	10	30	0-63	26	11-43
Microbial Limits ^a USP<61>, <62>	20	86	70-95	90	83-93
	(Q=80%) 30	97	91-103	96	94-99
	45	100	97-103	97	94-100
	Method Revision		01		01
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g		<50 cfu/g		N/A
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g		< 500 cfu/g		N/A
	Escherichia coli: Absent		Absent		N/A

FIG. 18

STORAGE		T= 0		30°C/85%RH
TEST DESCRIPTION				6 months
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y		Y
Dissolution (%LC) (Cores®-28602-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline			
	Time (min.)			
	10	%LC	Range	%LC
				Range
	20	34	0-66	27
		89	64-97	78
	30	100	88-105	94
	(Q=80%)			85-103
	45	103	99-106	98
				91-103
Microbial Limits ^a USP<61>, <62>	Trospium Chloride			
	Time (min.)			
	10	%LC	Range	%LC
				Range
	20	30	0-63	29
		86	70-95	80
	30	97	91-103	95
	(Q=80%)			91-103
	45	100	97-103	99
				95-103
Method Revision		01		01
Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g		<50 cfu/g		N/A
Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g		< 500 cfu/g		N/A
Escherichia coli: Absent		Absent		N/A

FIG. 19

STORAGE		T= 8		40°C/75%RH	
TEST DESCRIPTION		3 months		6 months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		N	
Dissolution (%LC) (Corrosion-28612-B-01) (n=6) (300 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline	Y		N	
	Time (min.)	Y		N	
	10	%LC	Range	%LC	Range
	20	34	0-86	27	3-58
	30	89	64-97	89	70-99
	45	100	88-105	97	87-103
	(Q=80%)	103	99-106	99	95-103
	Tropium Chloride	Y		N	
	Time (min.)	Y		N	
	10	%LC	Range	%LC	Range
Microbial Limits ^a USP<61>, <62>	20	30	0-83	26	2-59
	30	86	70-95	88	75-96
	45	97	91-103	94	87-98
	(Q=80%)	100	97-103	96	92-98
	Method Revision	01		01	
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A	
	Escherichia coli: Absent	Absent		N/A	

FIG. 20

Xanomeline API Related Substances Profile for Xanomeline/Trospium Cl 50/20 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months
Related Substances (%w/w) (n=1) (Corealis-28602-AD-01)	Unspecified impurity (RRT 0.24)	0.14	0.14	0.14
	Unspecified impurity (RRT 1.08)	0.20	0.14	0.18
	Method Revision	01	02	03

FIG. 21

Trospium Chloride API Related Substances Profile for Xanomeline/Trospium Cl 50/20 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months
Related Substances (%w/w) (n=1) (Corealis-28602-AD-01)	Unspecified impurity	Not Detected	Not Detected	Not Detected
	Method Revision	01	02	03

FIG. 22

Specification for Xanomeline/Trospium Cl 50/20 mg Capsules

TEST DESCRIPTION	ACCEPTANCE CRITERIA
	Stability, Rev 0
Description (Visual)	White to off-white opaque hard shell capsule with no markings
Water Content by KF (USP <921>, Method 1a)	Report result
Assay (%LC) (Corealis-28602-AD)	Xanomeline: 90 - 110% label claim (45 – 55 mg Xanomeline/capsule)
	Trospium Chloride: 90 - 110% label claim (18 – 22mg Trospium Chloride/capsule)
Related Substances (%LC)* (Corealis-28602-AD)	Trospium Chloride related compound B: NMT 0.2%LC
	Trospium Chloride related compound A: NMT 0.2%LC
	Any single unspecified impurity: NMT 0.2%LC
	Total Impurities: NMT 1.5%LC
Dissolution (Corealis-28602-B)	Xanomeline: NLT 80% (Q) of labeled amount of Xanomeline is dissolved at 30 minutes. Report profile
	Trospium Chloride: NLT 80% (Q) of labeled amount of Trospium Chloride is dissolved at 30 minutes. Report profile
Microbial Limits * USP<61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g
	Escherichia coli: Absent

FIG. 23

STORAGE		25°C/60%RH	
TEST DESCRIPTION		3 months	6 months
SPECIFICATION used at time of analysis		Stability, Rev 0	Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y	Y
Description (Visual)		Off-white opaque hard shell capsules with no markings	No change as compared to initials
Water content by KF (USP <921>, Method 1a) (n=3)	% w/w	2.4	1.8
Assay (Corruls-28602-AD-01) (n=2)	% label claim Xanomeline	102.0	103.7
	mg Xanomeline/capsule	76.5	77.8
	% label claim Trospium Chloride	95.9	97.9
	mg Trospium Chloride/capsule	9.6	9.8
	Method Revision	01	03
Related substances (HPLC) ^a (Corruls-28602-AD-01) (n=2)	Trospium Chloride related compound B	Not detected	Not detected
	Trospium Chloride related compound A	Not detected	Not detected
	Unspecified impurity (Xanomeline, PRTD 24) c, b	0.15	0.14
	Unspecified impurity (Xanomeline, PRT1, 10) c, b	0.15	0.20
	Total impurities	0.30	0.34
	Method Revision	01	03

FIG. 24

STORAGE		30°C/65%RH	
TEST DESCRIPTION		6 months	
SPECIFICATION used at time of analysis		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y	Y
Description (Visual)		Off-white opaque hard shell capsule with no markings	No change as compared to initials
Water content by KF (USP <921>, Method 1a) (n=3)	%w/w	2.4	2.2
Assay (Corealis-28602-AD-01) (n=2)	% label claim Xanomeline	102.0	102.8
	mg Xanomeline/capsule	76.5	77.1
	% label claim Trospium Chloride	95.9	96.0
	mg Trospium Chloride/capsule	9.6	9.6
	Method Revision	01	03
Related substances (%LC) ^a (Corealis-28602-AD-01) (n=2)	Trospium Chloride related compound B	Not detected	Not detected
	Trospium Chloride related compound A	Not detected	Not detected
	Unspecified impurity (Xanomeline_PRT0.24) c, b	0.15	0.14
	Unspecified impurity (Xanomeline_PRT1.10) c, b	0.15	0.24
	Total Impurities	0.30	0.38
	Method Revision	01	03

FIG. 25

STORAGE		40°C/75%RH	
TEST DESCRIPTION		3 months	6 months
SPECIFICATION used at time of analysis		Stability, Rev 0	Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y	N
Description (Visual)		Off-white opaque hard shell capsule with no markings	No change as compared to initials
Water content by KF (USP <921>, Method 1a) (n=3)	%w/w	2.4	2.3
Assay (Correlis-28502-AD-01) (n=2)	% label claim Xanomeline	102.0	103.3 ^F
	mg Xanomeline/capsule	76.5	77.5 ^F
	% label claim Trospium Chloride	95.9	98.7 ^F
	mg Trospium Chloride/capsule	9.6	9.9 ^F
	Method Revision	01	02
Related substances (NLC) ^A (Correlis-28502-AD-01) (n=2)	Trospium Chloride related compound B	Not detected	Not detected
	Trospium Chloride related compound A	Not detected	<0.1
	Unspecified impurity (Xanomeline_RRT0.24) c.b	0.15	0.14
	Unspecified impurity (Xanomeline_RRT1.10) c.b	0.15	0.20
	Total Impurities	0.30	0.34
	Method Revision	01	02

FIG. 26

STORAGE		T=0		25°C/60%RH			
TEST DESCRIPTION				3 months		6 months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y		Y	
Dissolution (%LC) (Corrals-28602-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline	%LC	Range	%LC	Range	%LC	Range
	Time (min.)						
	10	30	11-53	34	2-73	20	2-40
	20	87	79-98	89	69-103	97	83-103
	(Q=80%) 30	101	99-103	100	95-107	103	97-105
	45	104	103-105	103	99-107	104	102-105
	Trospium Chloride	%LC	Range	%LC	Range	%LC	Range
	Time (min.)						
	10	26	12-47	34	2-64	16	2-24
	20	84	74-91	86	70-100	93	84-104
Microbial Limits ^a USP<61>, <62>	(Q=80%) 30	98	93-103	94	89-104	100	95-107
	45	102	95-105	96	91-104	101	95-108
	Method Revision	01		01		01	
	Total Yeasts and Molds Counts (TYMC): 5100 cfu/g	<50 cfu/g		N/A		N/A	
	Total Aerobic Microbial Counts (TAMC): 51000 cfu/g	< 500 cfu/g		N/A		N/A	
Escherichia coli: Absent		Absent		N/A		N/A	

FIG. 27

STORAGE		T = 0		30°C/65%RH
TEST DESCRIPTION				6 months
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y		Y
Dissolution (%LC) (Criteria: 2802-B-01) (n=6) (500 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline			
	Time (min.)			
	10	%LC	Range	%LC
		30	11-53	24
	20	87	79-98	93
	(Q=80%) 30	101	89-103	102
	45	104	103-105	103
	Trospium Chloride			
	Time (min.)			
	10	%LC	Range	%LC
Microbial Limits ^a USP<61>, <62>		26	12-47	23
	20	84	74-91	91
	(Q=80%) 30	98	93-103	99
	45	102	95-105	99
	Method Revision	01		01
	Total Yeasts and Molds Counts (TYMC):	<50 cfu/g		N/A
	≤100 cfu/g			
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A
	Escherichia coli: Absent	Absent		N/A

FIG. 28

STORAGE		T= 0		40°C/75%RH	
TEST DESCRIPTION		3 months		6 months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		N	
Dissolution (%LC) (Correlis-28502-B-01) (n=6) (900 mL of 0.1N HCl, particles at 50 rpm)	Xanomeline Time (min.)	%LC	Range	%LC	Range ^f
	10	30	11-53	39	26
	20	87	79-98	95	85
	(Q=80%) 30	101	99-103	103	97
	45	104	103-105	104	100
	Trospium Chloride Time (min.)	%LC	Range	%LC	Range ^f
	10	26	12-47	36	24
	20	84	74-91	91	83
	(Q=80%) 30	98	93-103	98	94
	45	102	95-105	99	97
Method Revision		01		01	
Microbial Limits ^a USP<61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A	
	Escherichia coli Absent	Absent		N/A	

FIG. 29

Xanomeline API Related Substances Profile for Xanomeline/Trospium Cl 75/10 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months
Related Substances (%w/w) (n=1) (Corealis-28602-AD-01)	Unspecified impurity (PRT 0.23)	0.14	0.14	0.14
	Unspecified impurity (PRT 1.09)	0.20	0.14	0.21
	Method Revision	01	02	03

FIG. 30

Trospium Chloride API Related Substances Profile for Xanomeline/Trospium Cl 75/10 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months
Related Substances (%w/w) (n=1) (Corealis-28602-AD-01)	Unspecified impurity	Not Detected	Not Detected	Not Detected
	Method Revision	01	02	03

FIG. 31

Specification for Xanomeline/Trospium Cl 75/10 mg Capsules

TEST DESCRIPTION	ACCEPTANCE CRITERIA
	Stability, Rev 0
Description (Visual)	White to off-white opaque hard shell capsule with no markings
Water Content by KF (USP <921>, Method 1a)	Report result
Assay (%LC) (Corealis-28602-AD)	Xanomeline: 90 – 110% label claim (68 – 83 mg Xanomeline/capsule)
	Trospium Chloride: 90 – 110% label claim (9 – 11 mg Trospium Chloride/capsule)
Related Substances (%LC) ^A (Corealis-28602-AD)	Trospium Chloride related compound B: NMT 0.2%LC
	Trospium Chloride related compound A: NMT 0.2%LC
	Any single unspecified Impurity: NMT 0.2%LC
	Total Impurities: NMT 1.5%LC
Dissolution (Corealis-28602-B)	Xanomeline: NLT 80% (Q) of labeled amount of Xanomeline is dissolved at 30 minutes. Report profile
	Trospium Chloride: NLT 80% (Q) of labeled amount of Trospium Chloride is dissolved at 30 minutes. Report profile
Microbial Limits ^B USP<61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g
	Escherichia coli: Absent

FIG. 32

STORAGE		T=0		25°C/60%RH	
TEST DESCRIPTION		3 Months		6 Months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y	
Dissolution (%LC) (Corrosio-28602-B-01) (n=6) (900 mL of 0.1N HCl, packages at 50 rpm)	Xanomeline	Range		Range	
	Time (min.)	%LC		%LC	
	10	27		41	
	20	86		98	
	30	98		103	
	45	101		103	
	Tropism Chloride	Range		Range	
	Time (min.)	%LC		%LC	
	10	26		35	
	20	84		92	
Microbial Limits * USP<61>, <62>	(Q=80%) 30	86-104		101-105	
	45	91-105		102-105	
	Method Revision	01		01	
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A	
	Escherichia coli: Absent	Absent		N/A	

FIG. 33

STORAGE		30°C/65%RH	
TEST DESCRIPTION		T=0	
SPECIFICATION used at time of analysis		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y	
Dissolution (%LC) (Corrals-25802-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline Time (min.)	%LC	Range
	10	27	7-69
	20	88	74-99
	(Q=80%) 30	98	86-104
	45	101	91-105
	Tropium Chloride Time (min.)	%LC	Range
	10	26	7-85
	20	84	75-93
	(Q=80%) 30	95	89-101
	45	99	93-102
Method Revision		01	
Microbial Limits * USP <61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g	
	Escherichia coli: Absent	Absent	
		N/A	

FIG. 34

STORAGE		T= 0		40°C/75%RH			
TEST DESCRIPTION		Stability, Rev 0		3 Months Stability, Rev 0		6 Months Stability, Rev 0	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N) Description (Visual) Water content by KF (USP <921>, Method 1a) (n=3)		Y		Y		N	
		Off-white opaque hard shell capsule with no markings		No change as compared to initials		No change as compared to initials	
	%w/w	2.9		3.1		2.8	
	% label claim Xanomeline	102.1		102.8		102.9	
	mg Xanomeline/capsule	76.5		77.1		77.2	
	% label claim Trospium Chloride	94.6		101.3		95.4	
	mg Trospium Chloride/capsule	18.9		20.3		19.1	
	Method Revision	01		02		03	
	Trospium Chloride related compound B	Not detected		Not detected		Not detected	
	Trospium Chloride related compound A	Not detected		<0.1		0.14	
Related substances (%LC) ^ (Corasis-28502-AD-01) (n=2)	Unspecified impurity (Xanomeline, PRT0.24) c.b	0.15		0.14		0.14	
	Unspecified impurity (Xanomeline, PRT1.10) c.b	0.18		0.21		0.27*	
	Total Impurities	0.32		0.35		0.55	
	Method Revision	01		02		03	

FIG. 35

STORAGE		T= 0		25°C/60%RH	
TEST DESCRIPTION				3 Months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y	
Dissolution (%LC) (Concise 29802-B-01) (n=6) (900 mL of 0.1N HCl, packets at 50 rpm)	Xanomeline				
	Time (min.)				
	10	27	7-89	41	7-94
	20	86	74-99	99	94-105
	(Q=80%) 30	98	86-104	103	101-105
	45	101	91-105	103	102-105
	Tropium Chloride				
	Time (min.)	%LC	Range	%LC	Range
	10	26	7-65	35	5-82
	20	84	75-93	92	86-97
(Q=80%) 30	96	89-101	96	92-100	
45	99	93-102	96	93-100	
Method Revision		01		01	
Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g		<50 cfu/g		N/A	
Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g		< 500 cfu/g		N/A	
Escherichia coli: Absent		Absent		N/A	
Microbial Limits * USP <61>, <62>					

FIG. 36

STORAGE		T=0		30°C/65%RH	
TEST DESCRIPTION		Stability, Rev 0		8 Months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y	
Dissolution (%LC) (Corrosal-25002-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline Time (min.)	%LC	Range	%LC	Range
	10	27	7-69	16	5-46
	20	86	74-99	85	76-89
	(Q=80%) 30	98	86-104	99	96-101
	45	101	91-105	103	99-105
	Trospium Chloride Time (min.)	%LC	Range	%LC	Range
	10	26	7-65	12	5-34
	20	84	75-93	81	77-85
	(Q=80%) 30	96	89-101	94	92-96
	45	98	93-102	97	95-100
Method Revision		01		01	
Microbial Limits * USP<61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A	
	Escherichia coli: Absent	Absent		N/A	

FIG. 37

STORAGE		T=0		40°C/75%RH			
TEST DESCRIPTION		Stability, Rev 0		3 Months	6 Months		
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	Stability, Rev 0		
Conforms to acceptance criteria (Y/N)		Y		Y	N		
Dissolution (%LC) (Corrals-28802-B-01) (n=6) (300 ml of 0.1N HCl, paddles at 50 rpm)	Xanomeline Time (min.)	%LC	Range	%LC ^a	Range ^a	%LC	Range
	10	27	7-69	43	22-64	24	11-47
	20	86	74-99	91	71-100	93	78-100
	(Q=80%) 30	98	86-104	99	83-103	100	92-103
	45	101	91-105	100	84-103	102	98-104
	Trospium Chloride Time (min.)	%LC	Range	%LC ^a	Range ^a	%LC	Range
	10	26	7-65	39	18-67	24	9-45
	20	84	75-93	89	73-100	90	84-96
	(Q=80%) 30	96	89-101	96	90-105	97	92-100
	45	99	93-102	97	93-106	99	94-103
Method Revision		01		01	01	01	
Microbial Limits ^a USP<61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A		N/A	
	Escherichia coli: Absent	Absent		N/A		N/A	

FIG. 38

Xanomeline API Related Substances Profile for Xanomeline/Trospium Cl 75/20 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months
Related Substances (%w/w) (n=1) (Coreals-28602-AD-01)	Unspecified impurity (PRT 0.23)	0.14	0.14	0.14
	Unspecified impurity (PRT 1.09)	0.20	0.14	0.21
	Method Revision	01	02	03

FIG. 39

Trospium Chloride API Related Substances Profile for Xanomeline/Trospium Cl 75/20 Capsules

Stability time point		Initials	T= 3 months	T= 6 months
Related Substances (%w/w) (n=1) (Coreals-28602-AD-01)	Unspecified impurity	Not Detected	Not Detected	Not Detected
	Method Revision	01	02	03

FIG. 40

Specification for Xanomeline/Trospium Cl 75/20 mg Capsules

TEST DESCRIPTION	ACCEPTANCE CRITERIA
	Stability, Rev 0
Description (Visual)	White to off-white opaque hard shell capsule with no markings
Water Content by KF (USP <921>, Method 1a)	Report result
Assay (%LC) (Coreals-28602-AD)	Xanomeline: 90 - 110% label claim (68 – 83 mg Xanomeline/capsule)
	Trospium Chloride: 90 - 110% label claim (18 – 22mg Trospium Chloride/capsule)
Related Substances (%LC) ^a (Coreals-28602-AD)	Trospium Chloride related compound B: NMT 0.2%LC
	Trospium Chloride related compound A: NMT 0.2%LC
	Any single unspecified impurity: NMT 0.2%LC
	Total Impurities: NMT 1.5%LC
Dissolution (Coreals-28602-B)	Xanomeline: NLT 80% (Q) of labeled amount of Xanomeline is dissolved at 30 minutes. Report profile
	Trospium Chloride: NLT 80% (Q) of labeled amount of Trospium Chloride is dissolved at 30 minutes. Report profile
Microbial Limits ^b USP<61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g
	Escherichia coli: Absent

FIG. 41

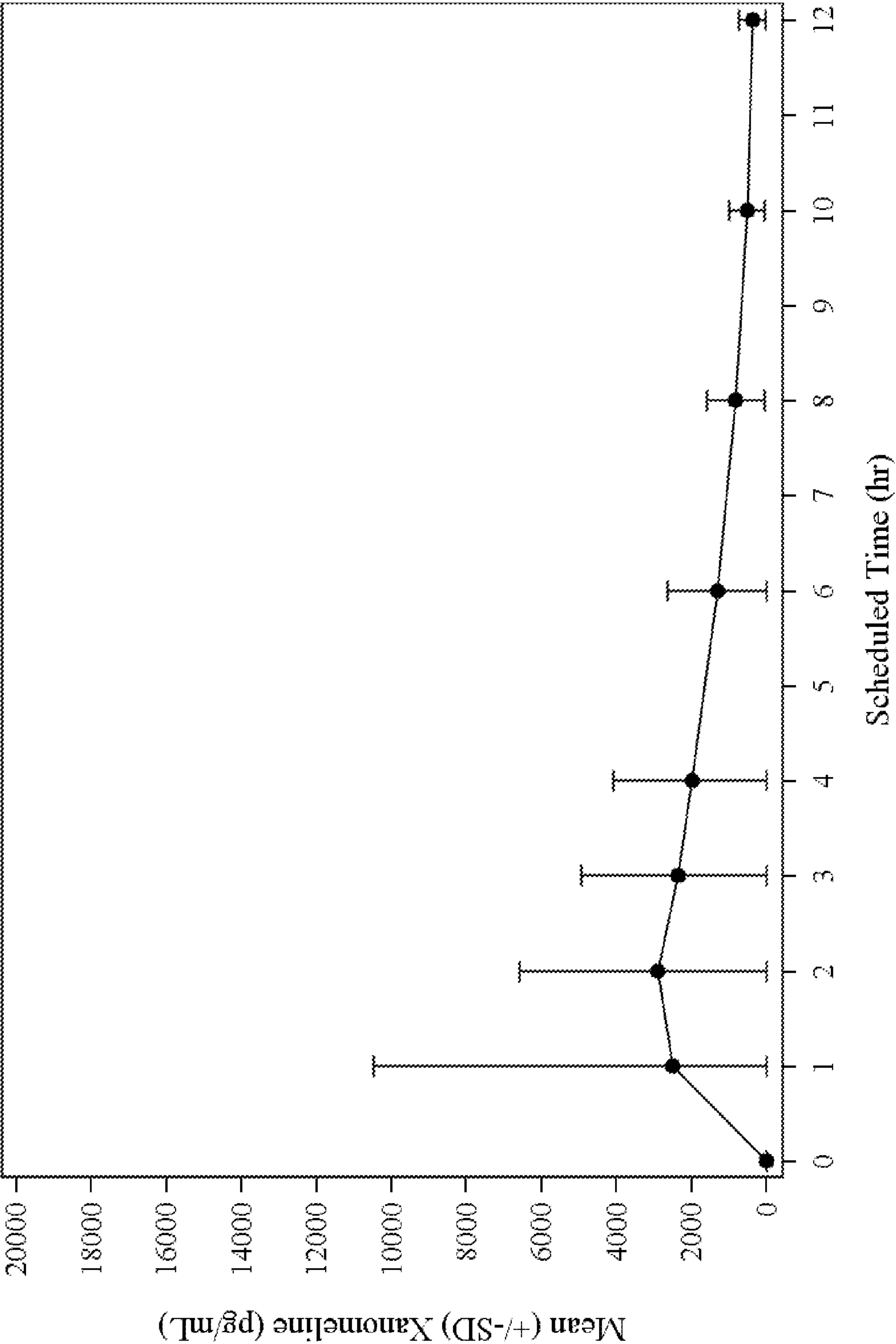


FIG. 42

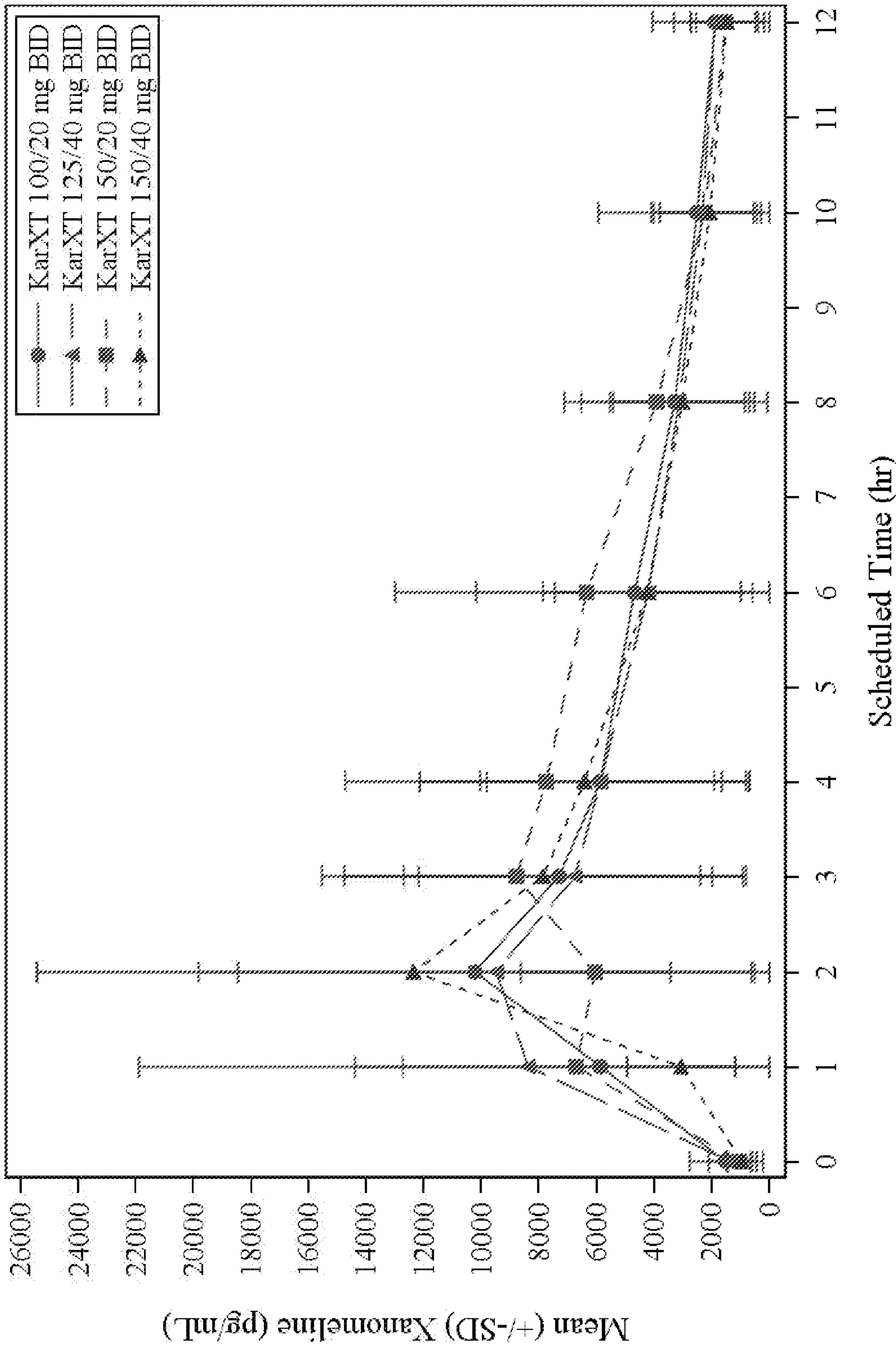


FIG. 43

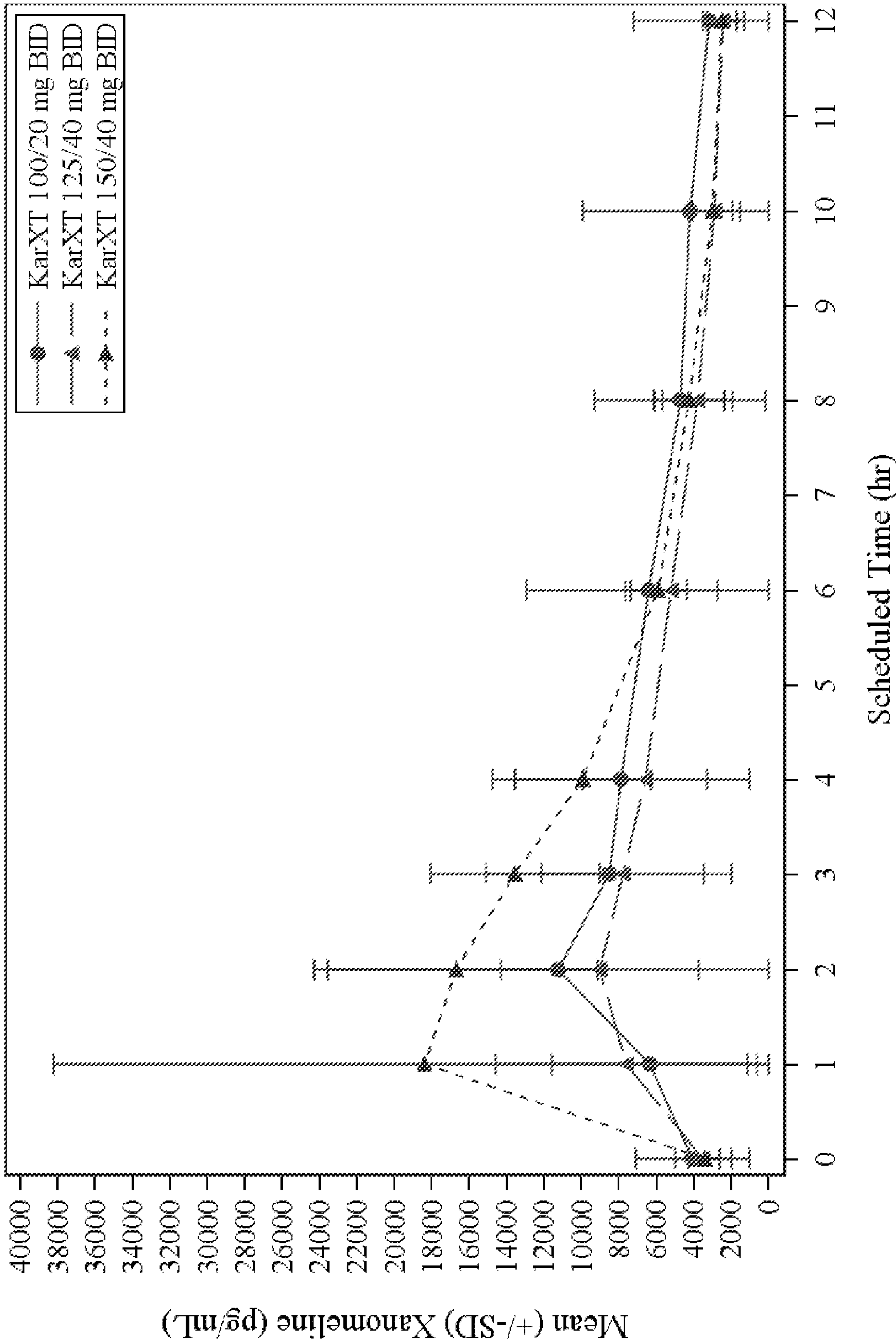


FIG. 44

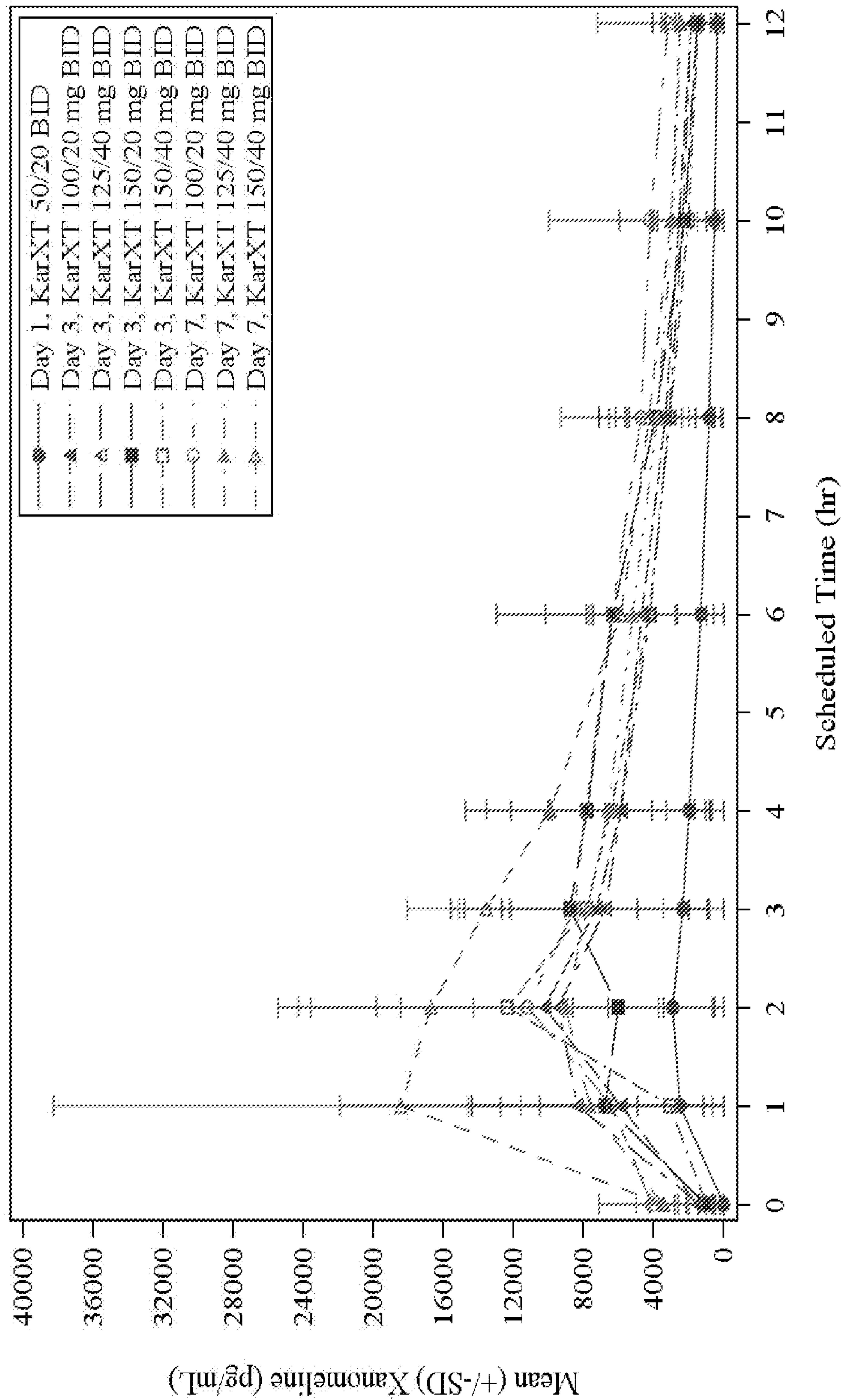


FIG. 45

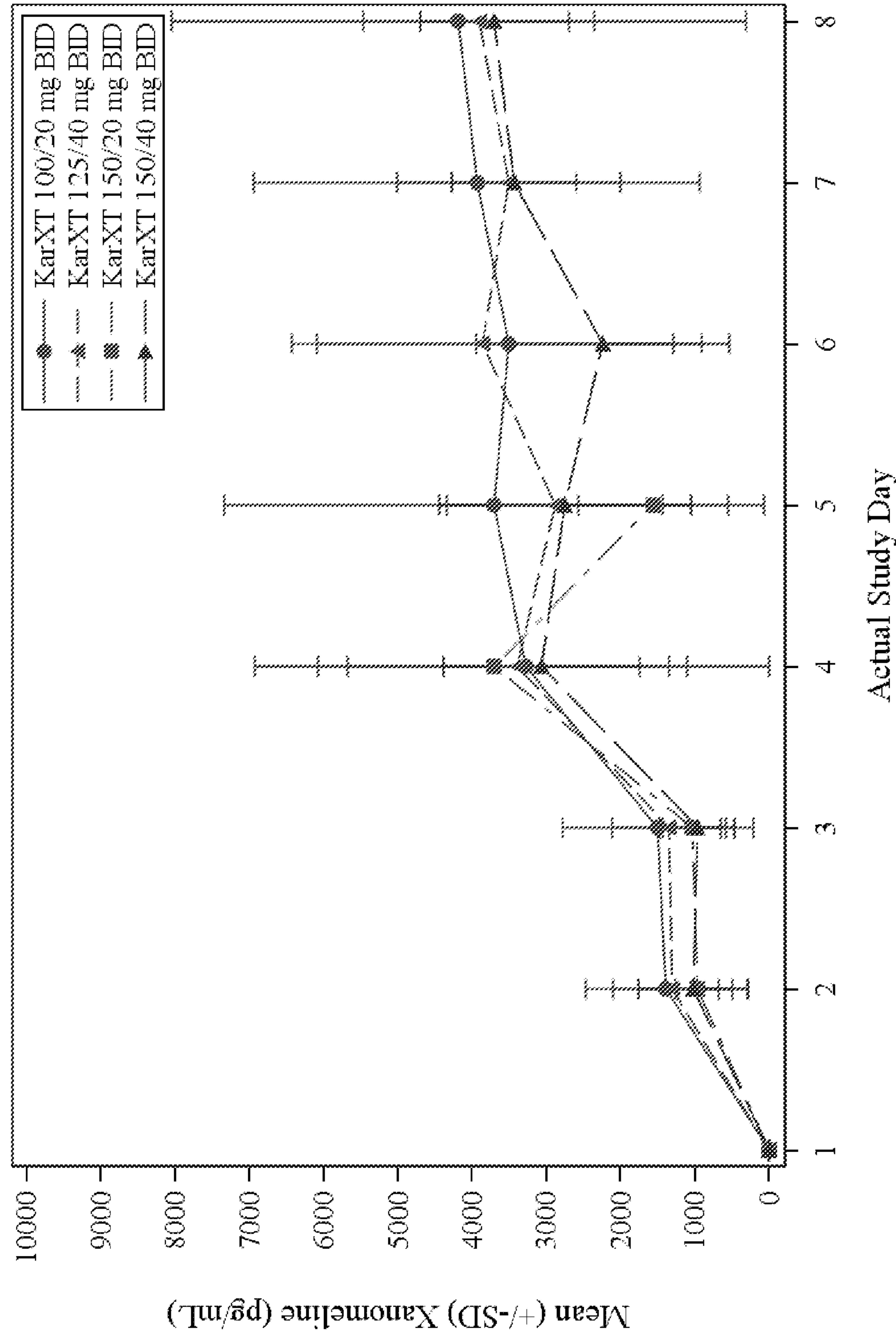


FIG. 46

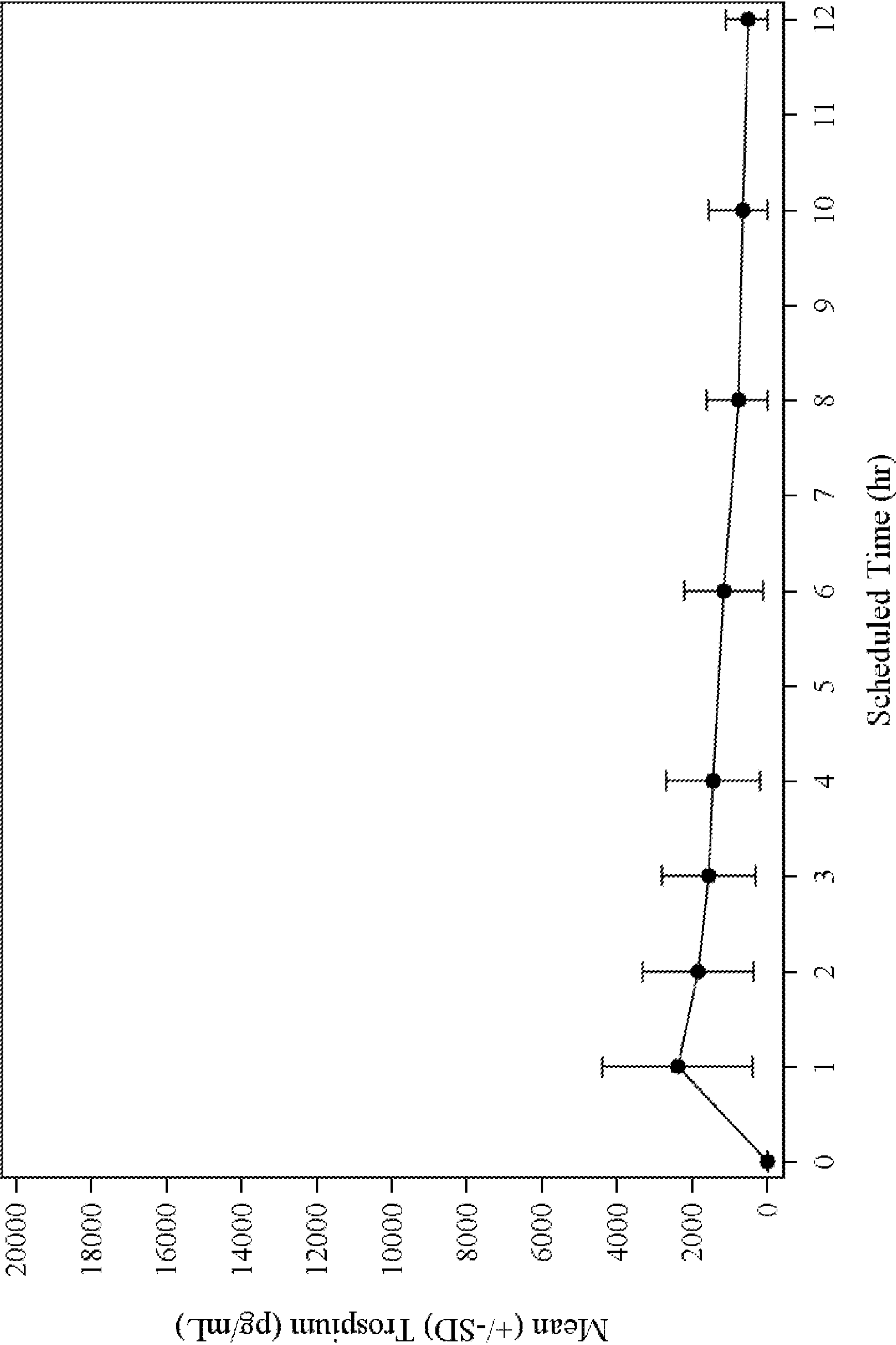


FIG. 47

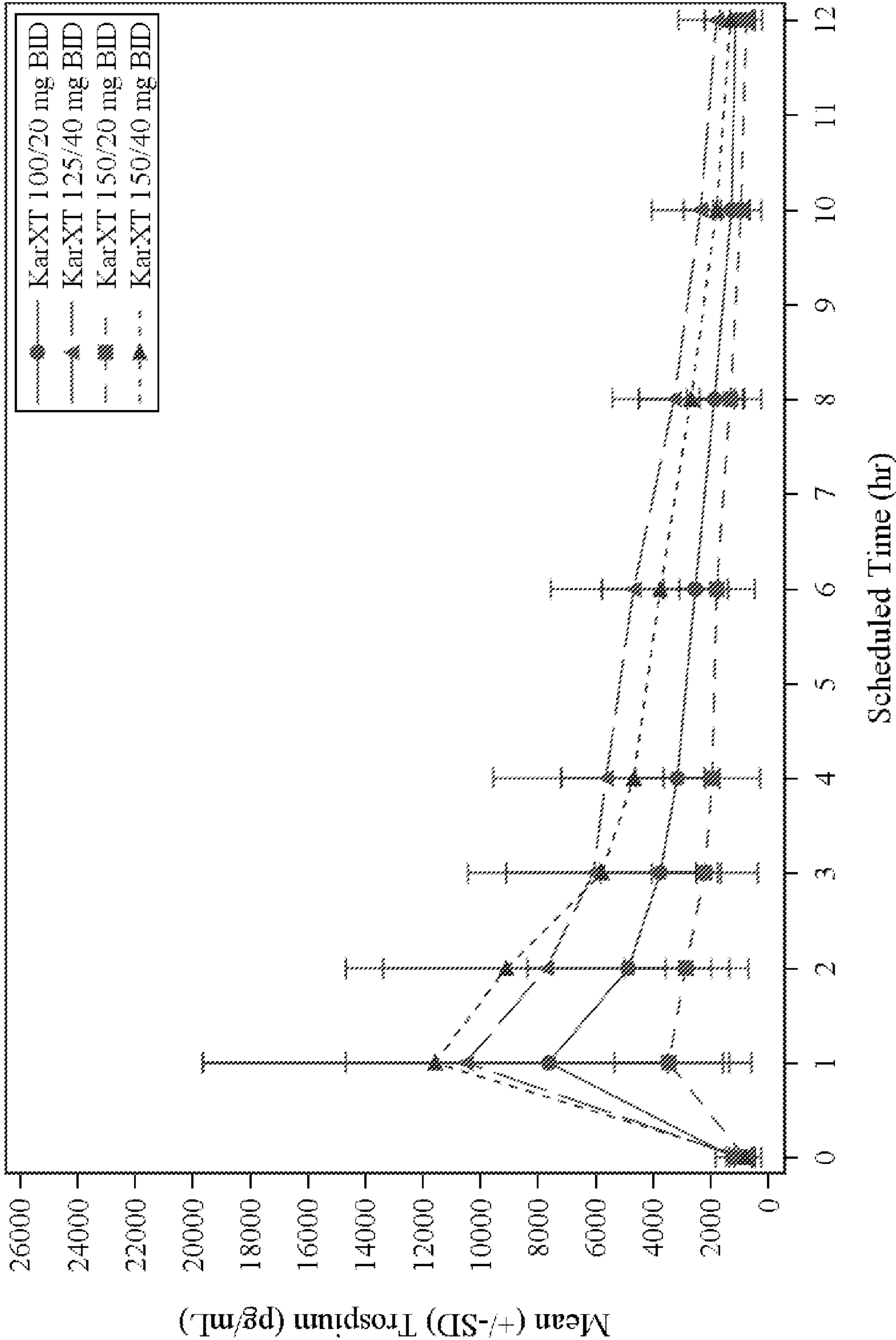


FIG. 48

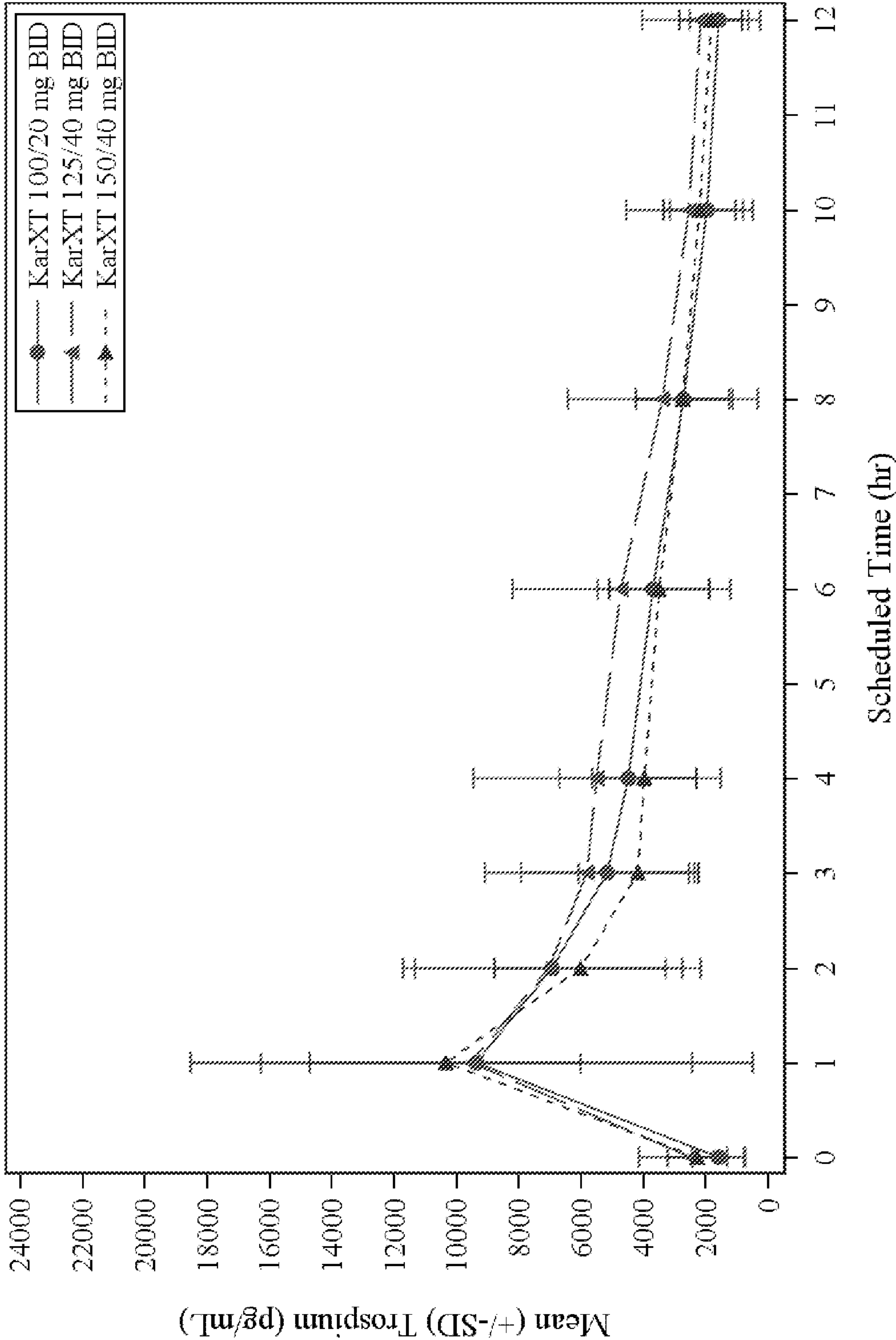


FIG. 49

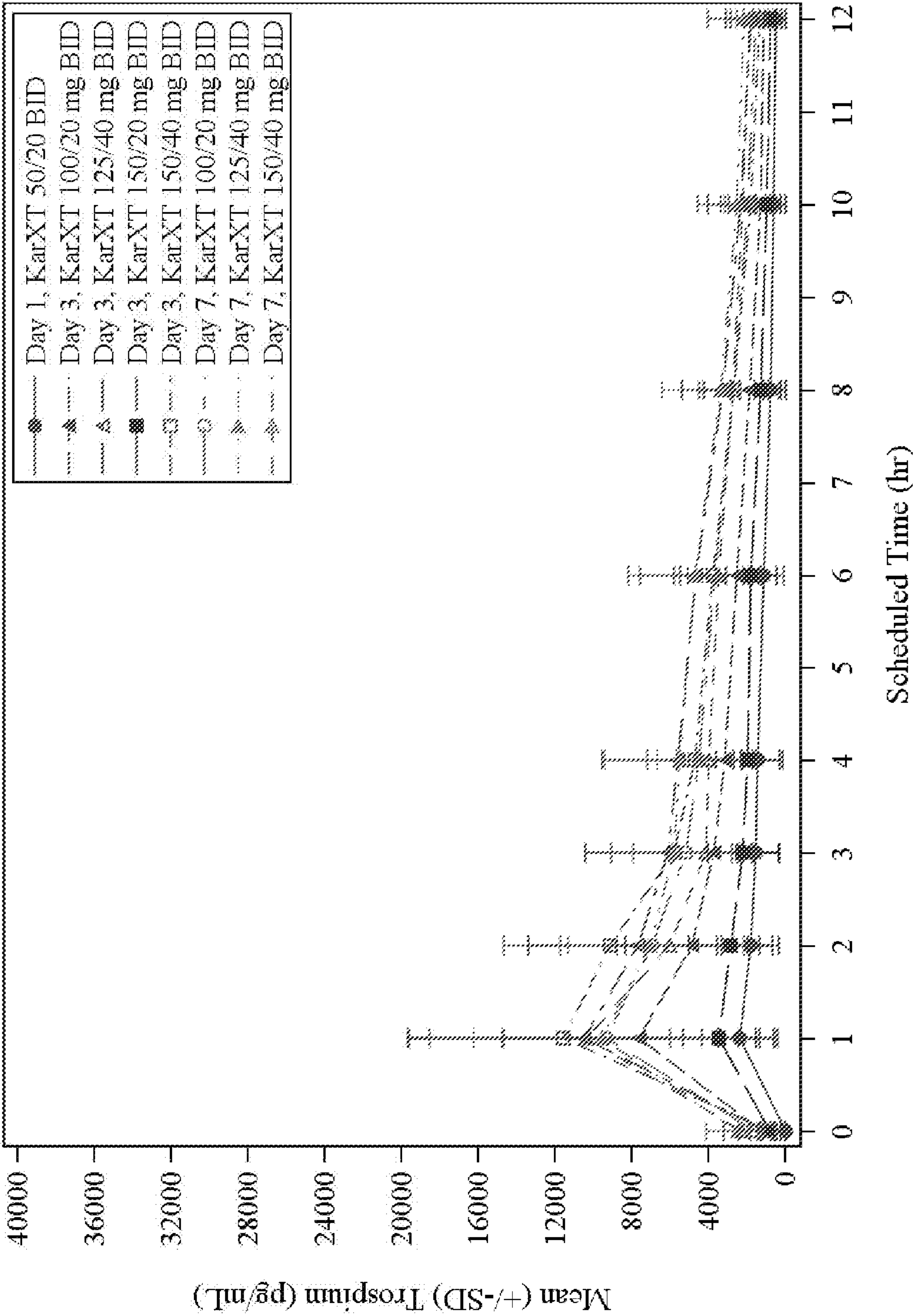


FIG. 50

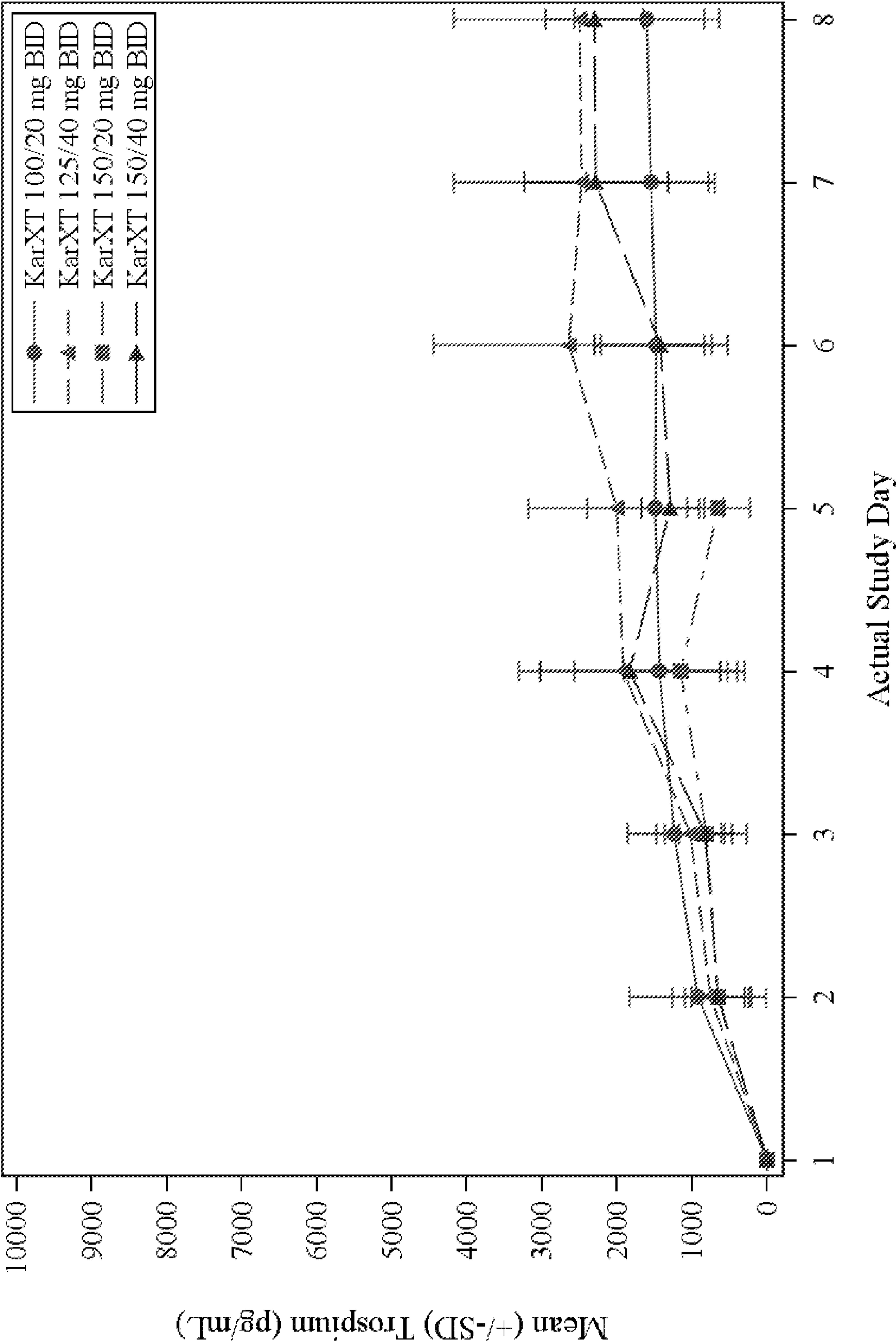


FIG. 51