COREALS Pharma

Stability protocol for Xanomeline / Trospuim 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) Trospuim 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) Trospuim 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

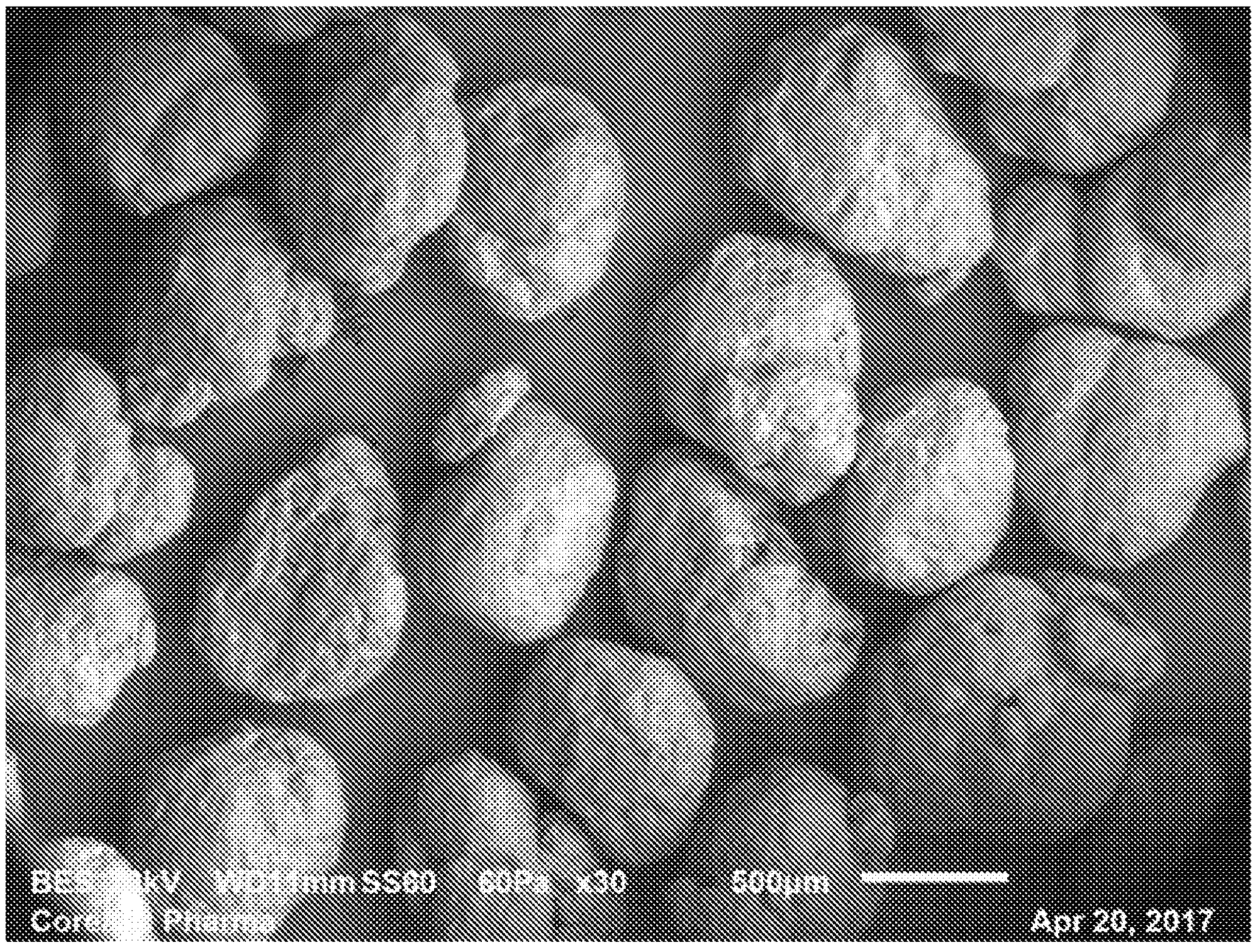

FIG 2

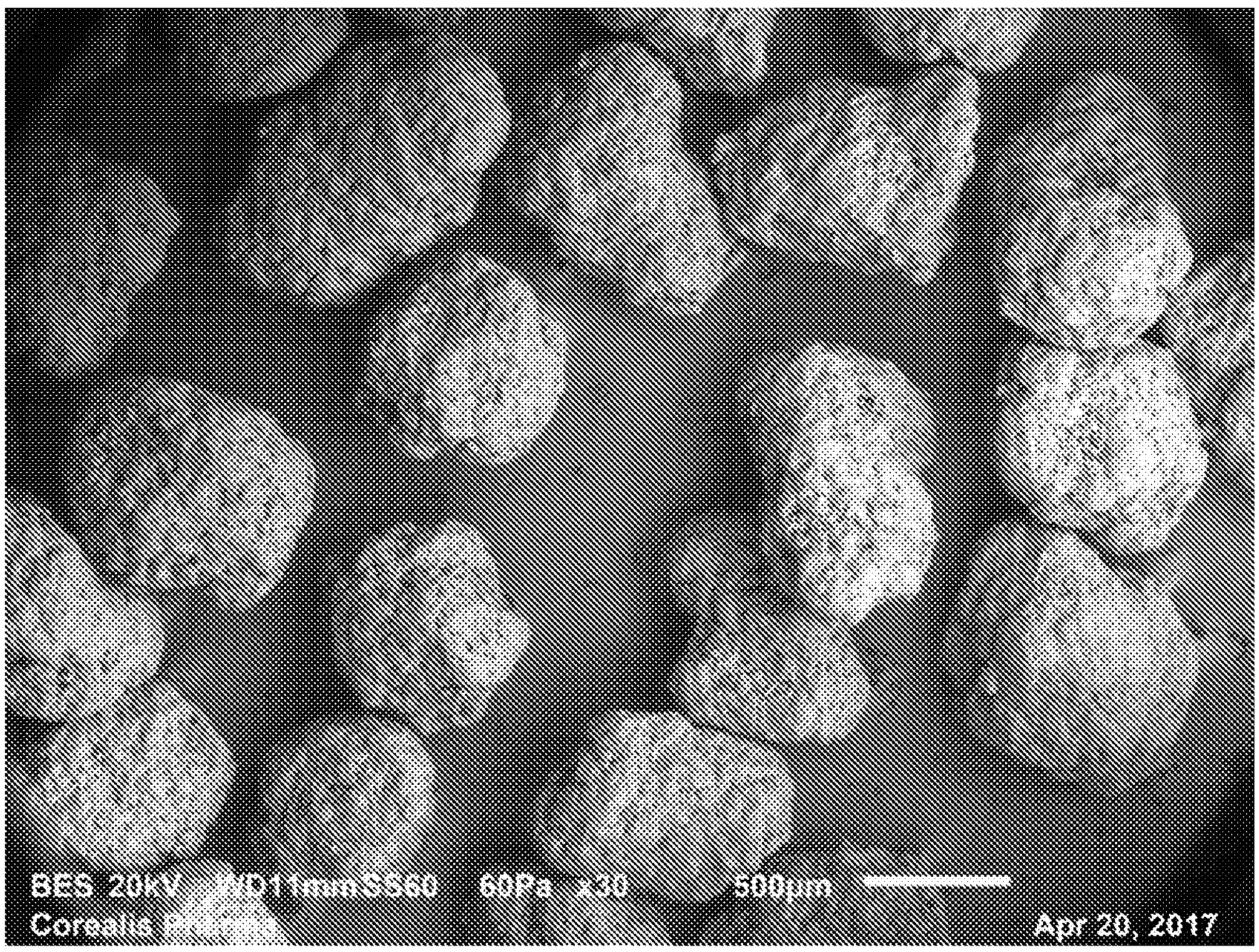

FIG. 3

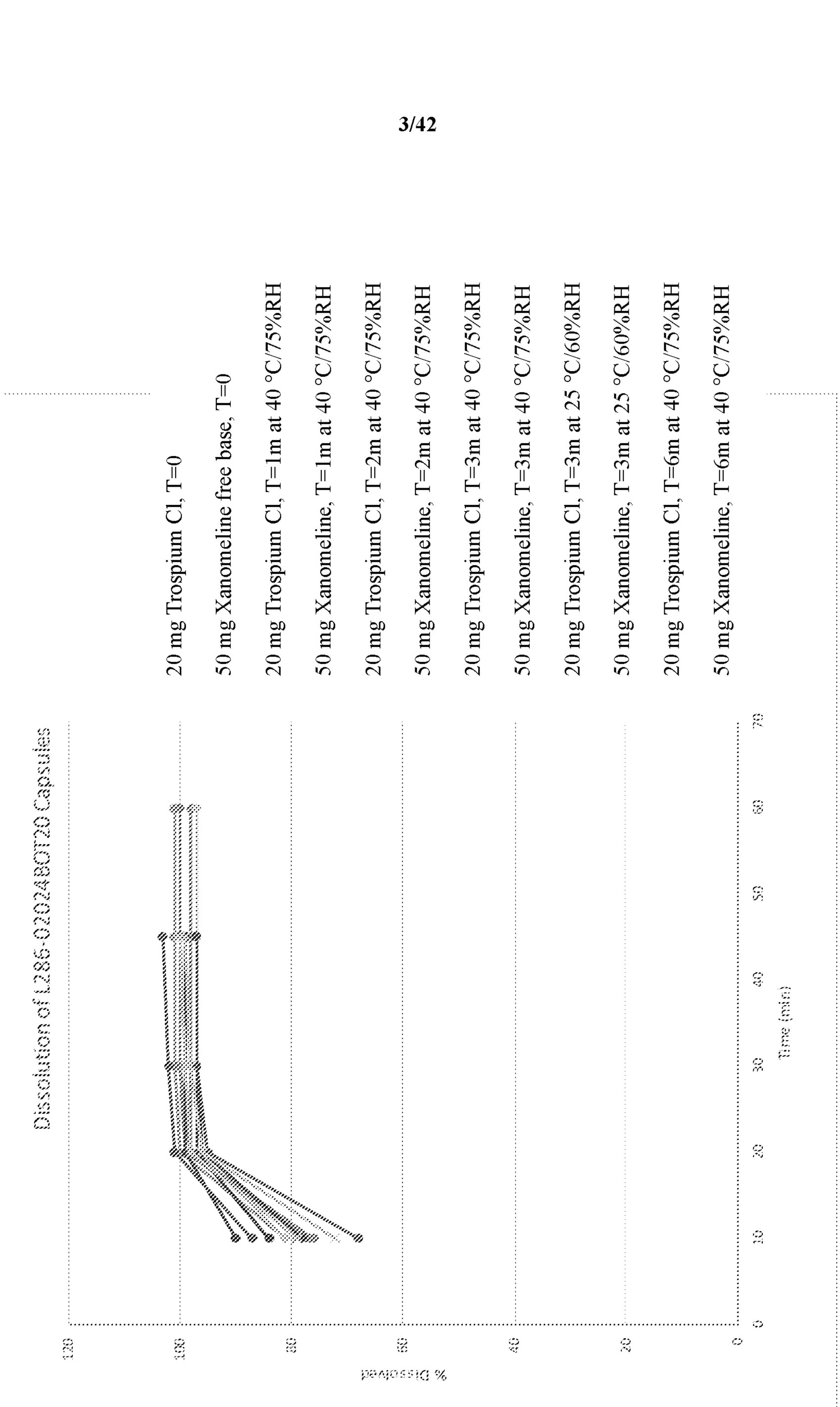
Dissolution of L286-02024BOT20 Capsules
% Dissolved
Time (min)
0
20
40
60
80
100
120
0
10
20
30
40
50
60
70
20 mg Trospium Cl, T=0
50 mg Xanomeline free base, T=0
20 mg Trospium Cl, T=1m at 40 °C/75%RH
50 mg Xanomeline, T=1m at 40 °C/75%RH
20 mg Trospium Cl, T=2m at 40 °C/75%RH
50 mg Xanomeline, T=2m at 40 °C/75%RH
20 mg Trospium Cl, T=3m at 40 °C/75%RH
50 mg Xanomeline, T=3m at 40 °C/75%RH
20 mg Trospium Cl, T=3m at 25 °C/60%RH
50 mg Xanomeline, T=3m at 25 °C/60%RH
20 mg Trospium Cl, T=6m at 40 °C/75%RH
50 mg Xanomeline, T=6m at 40 °C/75%RH

FIG. 4

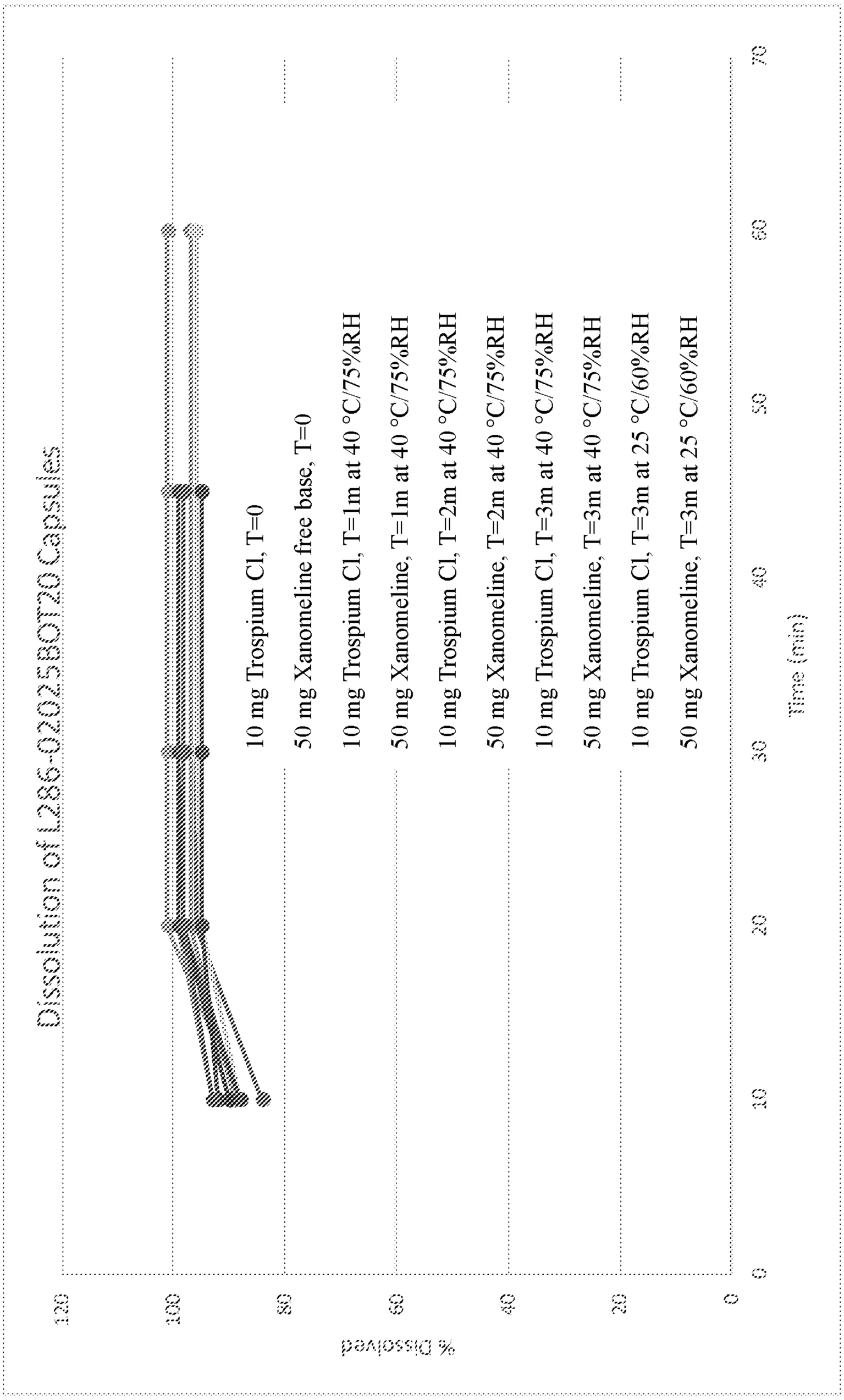
Dissolution of L286-0220 Capsules
10 mg Trospium Cl, T=0
50 mg Xanomeline free base, T=0
10 mg Trospium Cl, T=1m at 40 °C/75%RH
50 mg Xanomeline, T=1m at 40 °C/75%RH
10 mg Trospium Cl, T=2m at 40 °C/75%RH
50 mg Xanomeline, T=2m at 40 °C/75%RH
10 mg Trospium Cl, T=3m at 40 °C/75%RH
50 mg Xanomeline, T=3m at 40 °C/75%RH
10 mg Trospium Cl, T=3m at 25 °C/60%RH
50 mg Xanomeline, T=3m at 25 °C/60%RH
% Dissolved
0
20
40
60
80
100
120
10
20
30
40
50
60
Time (min)

FIG. 5

STORAGE		T= 0	25°C/60%RH		
TEST DESCRIPTION			3 Months	6 Months	9 Months
SPECIFICATION used at time of analysis		Release, Rev 0	Stability, Rev 01	Stability, Rev 01	Stability, Rev 01
Conforms to acceptance criteria (Y/N)		Y	Y	Y	Y
Description (Visual)		Off-white opaque hard shell capsule with no markings	No change as compared to initials	No change as compared to initials	No change as compared to initials
Water content by KF (USP <921>, Method 1a) (n=3)	%w/w	2.4	2.6	2.5	2.1
Assay (Consilx-29502-AD-01) (n=2)	% label claim Xanomeline	104.5 [C]	99.8	102.3	102.3
	mg Xanomeline/capsule	62.3 [C]	49.9	51.2	51.2
	% label claim Trospium Chloride	97.5 [C]	97.7	99.6	97.8
	mg Trospium Chloride/capsule	9.8 [C]	9.8	10.0	9.8
	Method Revision	0	01	02	03
Related substances (%LC) [A, B] (Consilx-29502-AD-01) (n=2)	Trospium Chloride related compound B	Not detected [C]	Not detected	Not detected	Not detected
	Trospium Chloride related compound A	Not detected [C]	<0.1	Not detected	Not detected
	Unspecified impurity (Xanomeline_RRT0.23) [C, D]	0.15 [C]	0.14	0.14	0.14
	Unspecified impurity (Xanomeline_RRT1.05) [C, D]	-	0.18	0.16	0.24
	Total Impurities	0.15 [C]	0.32 [D]	0.30	0.37
	Method Revision	0	01	02	03

FIG. 6

STORAGE		T= 0	30°C/65%RH	
TEST DESCRIPTION			3 Months	6 Months
SPECIFICATION used at time of analysis		Release, Rev 0	Stability, Rev 01	Stability, Rev 01
		7-0138		9
Conforms to acceptance criteria (Y/N)		Y	Y	Y
Description *(Visual)*		Off-white opaque hard shell capsule with no markings	No change as compared to initials	No change as compared to initials
Water content by KF *(USP <921>, Method 1a) (n=3)*	%w/w	2.4	2.5	2.7
Assay *(Corealis-28602-AD-01) (n=2)*	% label claim Xanomeline	104.5 [C]	100.6	102.3
	mg Xanomeline/capsule	52.3 [C]	50.3	51.2
	% label claim Trospium Chloride	97.5 [C]	98.4	98.0
	mg Trospium Chloride/capsule	9.8 [C]	9.8	9.8
	Method Revision	0	01	02
Related substances (%LC)[A] *(Corealis-28602-AD-01) (n=2)*	Trospium Chloride related compound B	Not detected [C]	Not detected	Not detected
	Trospium Chloride related compound A	Not detected [C]	Not detected	Not detected
	Unspecified Impurity (Xanomeline_RRT0.24) [E,F]	0.15 [C]	0.14	0.14
	Unspecified Impurity (Xanomeline_RRT1.09) [E,F]	-	0.18	0.19
	Total Impurities	0.15 [C]	0.30	0.33
	Method Revision	0	01	02

FIG. 7

STORAGE		T= 0	40°C/75%RH	
TEST DESCRIPTION			3 Months	6 Months
SPECIFICATION used at time of analysis		Release, Rev 0	Stability, Rev 01	Stability, Rev 01
		0136		
Conforms to acceptance criteria (Y/N)		Y	Y	Y
Description *(Visual)*		Off-white opaque hard shell capsule with no markings	No change as compared to initials	No change as compared to initials
Water content by KF *(USP <921>, Method Ia) (n=3)*	%w/w	2.4	2.5	2.9
Assay *(Console-28602-AD-01) (n=2)*	% label claim Xanomeline	104.5 [c]	99.3	101.7
	mg Xanomeline/capsule	52.3 [c]	49.6	50.9
	% label claim Trospium Chloride	97.5 [c]	97.0	100.4
	mg Trospium Chloride/capsule	9.8 [c]	9.7	10.0
	Method Revision	0	01	02
Related substances (%LC) [a] *(Console-28602-AD-01) (n=2)*	Trospium Chloride related compound B	Not detected [c]	Not detected	Not detected
	Trospium Chloride related compound A	Not detected [c]	Not detected	0.19
	Unspecified Impurity (Xanomeline_RRT0.24) [d,b]	0.15 [c]	0.14	0.14
	Unspecified Impurity (Xanomeline_RRT1.09) [d,a]	-	0.14	0.22
	Total Impurities	0.15 [c]	0.28	0.55
	Method Revision	0	01	02

FIG. 8

STORAGE		T= 0		25°C/60%RH					
TEST DESCRIPTION				3 Months		6 Months		9 Months	
SPECIFICATION used at time of analysis		Release, Rev 0		Stability, Rev 01		Stability, Rev 01		Stability, Rev 01	
		9138				90[illegible]			
Conforms to acceptance criteria (Y/N)		Y		Y		Y		Y	
Dissolution (%LC) (Consult-ZRSOL-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline Time (min.)	%LC	Range	%LC	Range	%LC[a]	Range[a]	%LC	Range
	10	54	12-89	30	7-67	34	1-74	47	28-62
	20	98	90-102	95	75-97	89	82-101	98	95-102
	(Q=80%) 30	103	102-104	100	98-101	99	97-102	101	99-103
	45	103	103-104	102	101-103	102	99-103	101	101-102
	Trospium Chloride Time (min.)	%LC	Range	%LC	Range	%LC[a]	Range[a]	%LC	Range
	10	48	11-83	27	6-60	32	0-65	43	23-63
	20	93	87-98	85	75-89	86	66-97	95	89-100
	(Q=80%) 30	96	94-102	97	92-103	85	81-100	98	94-104
	45	96	94-102	99	95-103	97	90-104	99	96-104
	Method Revision	0		01		01		01	
Microbial Limits[b] USP<61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A		N/A		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A		N/A		N/A	
	Escherichia coli: Absent	Absent		N/A		N/A		N/A	

FIG. 9

STORAGE		T= 0		30°C/65%RH			
TEST DESCRIPTION				3 Months		6 Months	
SPECIFICATION used at time of analysis		Release, Rev 0		Stability, Rev 01		Stability, Rev 01	
		7-0138					
Conforms to acceptance criteria (Y/N)		Y		Y		Y	
Dissolution (%LC) (Corealis-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	54	12-89	35	14-58	35	3-64
	20	98	90-102	85	69-96	97	89-103
	(Q=80%) 30	103	102-104	101	99-103	102	100-104
	45	103	103-104	102	100-104	103	101-104
	Trospium Chloride	%LC	Range	%LC	Range	%LC	Range
	Time (min.)						
	10	49	11-83	30	9-54	30	2-56
	20	93	87-98	84	68-93	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	
Microbial Limits [8] 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. 10

STORAGE		T= 0		40°C/75%RH			
TEST DESCRIPTION				3 Months		6 Months	
SPECIFICATION used at time of analysis		Release, Rev 0		Stability, Rev 01		Stability, Rev 01	
		-0136					
Conforms to acceptance criteria (Y/N)		Y		Y		Y	
Dissolution (%LC) (Corealis-28602-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50rpm)	Xanomeline	%LC	Range	%LC	Range	%LC	Range
	Time (min.)						
	10	54	12-89	45	6-90	45	17-90
	20	98	90-102	89	80-99	89	71-101
	(Q=80%) 30	103	102-104	98	93-101	97	93-101
	45	103	103-104	100	98-101	99	97-101
	Trospium Chloride	%LC	Range	%LC	Range	%LC	Range
	Time (min.)						
	10	49	11-83	42	3-85	40	17-71
	20	93	87-98	86	74-94	87	75-96
	(Q=80%) 30	96	94-102	95	87-101	95	91-99
	45	96	94-102	97	92-103	97	93-100
	Method Revision	0		01		01	
Microbial Limits* 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. 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) (Consilx-28602-AO-01)	Unspecified impurity (RRT 0.23)	0.14	0.14	0.14	0.14
	Unspecified impurity (RRT 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) (Consilx-28602-AO-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 Release, Rev 0	ACCEPTANCE CRITERIA 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) (Consilx-28602-AO)	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)* (Consilx-28602-AO)	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 (Consilx-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* 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	Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y	Y	Y
Description *(Visual)*		Off-white opaque hard shell capsule with no markings	No change as compared to initials	No change as compared to initials
Water content by KF *(USP <921>, Method 1a)* *(n=3)*	%w/w	2.9	2.7	3.0
Assay *(Coreaks-26602-AD-01)* *(n=2)*	% label claim Xanomeline	101.8	101.9	102.2
	mg Xanomeline/capsule	50.9	51.0	51.1
	% label claim Trospium Chloride	98.3	98.2	98.3
	mg Trospium Chloride/capsule	19.7	19.6	19.7
	Method Revision	01	02	03
Related substances (%LC)[4] *(Coreaks-26602-AD-01)* *(n=2)*	Trospium Chloride related compound B	Not detected	Not detected	Not detected
	Trospium Chloride related compound A	Not detected	Not detected	Not detected
	Unspecified Impurity (Xanomeline_RRT0.23) [5,6]	0.13	0.14	0.14
	Unspecified Impurity (Xanomeline_RRT1.09) [5,6]	0.17	0.14	0.20
	Total Impurities	0.30	0.28	0.34
	Method Revision	01	02	03

FIG. 15

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
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	2.9	3.0
Assay *(Corealis-28602-AD-01)* *(n=2)*	% label claim Xanomeline	101.8	101.5
	mg Xanomeline/capsule	50.9	50.8
	% label claim Trospium Chloride	98.3	96.4
	mg Trospium Chloride/capsule	19.7	19.3
	Method Revision	01	03
Related substances (%LC)[4] *(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_RRT0.23)[C, D]	0.13	0.14
	Unspecified Impurity (Xanomeline_RRT1.09)[C, D]	0.17	0.23
	Total Impurities	0.30	0.37
	Method Revision	01	03

FIG. 16

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	Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y	Y	N
Description *(Visual)*		Off-white opaque hard shell capsule with no markings	No change as compared to initials	No change as compared to initials
Water content by KF *(USP <921>, Method 1a)* *(n=3)*	%w/w	2.9	2.9	3.1
Assay *(Corealis-28602-AD-01)* *(n=2)*	% label claim Xanomeline	101.8	101.8	100.9
	mg Xanomeline/capsule	50.9	50.9	50.5
	% label claim Trospium Chloride	98.3	98.1	96.2
	mg Trospium Chloride/capsule	19.7	19.6	19.2
	Method Revision	01	02	03
Related substances (%LC)[4] *(Corealis-28602-AD-01)* *(n=2)*	Trospium Chloride related compound B	Not detected	Not detected	Not detected
	Trospium Chloride related compound A	Not detected	<0.1	0.14
	Unspecified Impurity (Xanomeline_RRT0.23) [c, d]	0.13	0.14	0.14
	Unspecified Impurity (Xanomeline_RRT1.08) [c, d]	0.17	0.20	0.28[5]
	Total Impurities	0.30	0.33	0.54
	Method Revision	01	02	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) (Coreaks-28602-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline Time (min.)	%LC	Range	%LC	Range	%LC	Range
	10	34	0-66	27	11-46	29	0-71
	20	89	64-97	94	85-101	77	66-97
	(Q=80%) 30	100	88-105	102	99-105	98	88-102
	45	103	99-106	103	99-105	102	99-107
	Trospium Chloride Time (min.)	%LC	Range	%LC	Range	%LC	Range
	10	30	0-63	26	11-43	29	0-66
	20	86	70-95	90	83-93	75	62-92
	(Q=80%) 30	97	91-103	96	94-99	94	87-99
	45	100	97-103	97	94-100	98	95-101
	Method Revision	01		01		01	
Microbial Limits[8] 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. 18

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) *(Corealis-28602-8-01)* *(n=6)* *(900 mL of 0.1N HCl, paddles at 50 rpm)*	Xanomeline Time (min.)	%LC	Range	%LC	Range
	10	34	0-66	27	6-48
	20	89	64-97	78	60-99
	(Q=80%) 30	100	88-105	94	85-103
	45	103	99-106	98	91-103
	Trospium Chloride Time (min.)	%LC	Range	%LC	Range
	10	30	0-63	29	6-49
	20	86	70-95	80	65-101
	(Q=80%) 30	97	91-103	95	91-103
	45	100	97-103	99	95-103
	Method Revision	01		01	
Microbial Limits[8] *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. 19

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		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y		N	
Dissolution (%LC) (Corealis-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	34	0-66	27	3-58	32	10-56
	20	89	64-97	89	70-99	94	75-101
	(Q=80%) 30	100	88-105	97	87-103	99	93-102
	45	103	99-106	99	95-103	100	97-102
	Trospium Chloride	%LC	Range	%LC	Range	%LC	Range
	Time (min.)						
	10	30	0-63	26	2-59	28	8-45
	20	86	70-95	88	75-96	93	79-98
	(Q=80%) 30	97	91-103	94	87-98	98	96-100
	45	100	97-103	96	92-98	99	98-101
	Method Revision	01		01		01	
Microbial Limits[a] USP<61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		NA		NA	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		NA		NA	
	Escherichia coli: Absent	Absent		NA		NA	

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) (Cereals-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) (Cereals-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) (Cereals-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)* (Cereals-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 (Cereals-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		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
Description *(Visual)*		Off-white opaque hard shell capsule with no markings	No change as compared to initials	No change as compared to initials
Water content by KF *(USP <921>, Method 1a) (n=3)*	%w/w	2.4	2.3	1.8
Assay *(Corealis-28602-AD-01) (n=2)*	% label claim Xanomeline	102.0	104.6	103.7
	mg Xanomeline/capsule	76.5	78.4	77.8
	% label claim Trospium Chloride	95.9	98.7	97.9
	mg Trospium Chloride/capsule	9.6	9.9	9.8
	Method Revision	01	02	03
Related substances (%LC)[A] *(Corealis-28602-AD-01) (n=2)*	Trospium Chloride related compound B	Not detected	Not detected	Not detected
	Trospium Chloride related compound A	Not detected	Not detected	Not detected
	Unspecified Impurity (Xanomeline_RRT0.24)[C, D]	0.15	0.14	0.14
	Unspecified Impurity (Xanomeline_RRT1.10)[C, D]	0.15	0.13	0.20
	Total Impurities	0.30	0.27	0.34
	Method Revision	01	02	03

FIG. 24

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
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_RRT0.24)[C, D]	0.15	0.14
	Unspecified Impurity (Xanomeline_RRT1.10)[C, D]	0.15	0.24
	Total Impurities	0.30	0.38
	Method Revision	01	03

FIG. 25

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	Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y	Y	N
Description *(Visual)*		Off-white opaque hard shell capsule with no markings	No change as compared to initials	No change as compared to initials
Water content by KF *(USP <921>, Method 1a)* *(n=3)*	%w/w	2.4	2.3	2.3
Assay *(Coreaks-28602-AD-01)* *(n=2)*	% label claim Xanomeline	102.0	103.3[5]	101.8
	mg Xanomeline/capsule	76.5	77.5[5]	76.3
	% label claim Trospium Chloride	95.9	98.7[5]	94.3
	mg Trospium Chloride/capsule	9.6	9.9[5]	9.4
	Method Revision	01	02	03
Related substances (%LC)[4] *(Coreaks-28602-AD-01)* *(n=2)*	Trospium Chloride related compound B	Not detected	Not detected	Not detected
	Trospium Chloride related compound A	Not detected	<0.1	0.16
	Unspecified Impurity (Xanomeline_RRT0.24)[6,8]	0.15	0.14	0.14
	Unspecified Impurity (Xanomeline_RRT1.10)[6,8]	0.15	0.20	0.28[9]
	Total Impurities	0.30	0.34	0.56
	Method Revision	01	02	03

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) *(Corealis-28602-B-01)* *(n=6)* *(900 mL of 0.1N HCl, paddles at 50 rpm)*	Xanomeline Time (min.)	%LC	Range	%LC	Range	%LC	Range
	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	96-107	103	97-106
	45	104	103-105	103	99-107	104	102-105
	Trospium Chloride Time (min.)	%LC	Range	%LC	Range	%LC	Range
	10	26	12-47	34	2-64	16	2-24
	20	84	74-91	86	70-100	93	84-104
	(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	
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. 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) *(Corealis-28602-B-01)* *(n=6)* *(900 mL of 0.1N HCl, paddles at 50 rpm)*	Xanomeline	%LC	Range	%LC	Range
	Time (min.)				
	10	30	11-53	24	0-48
	20	87	79-98	93	86-101
	(Q=80%) 30	101	99-103	102	101-103
	45	104	103-105	103	102-104
	Trospium Chloride	%LC	Range	%LC	Range
	Time (min.)				
	10	26	12-47	23	0-44
	20	84	74-91	91	87-94
	(Q=80%) 30	98	93-103	99	96-106
	45	102	95-105	99	96-107
	Method Revision	01		01	
Microbial Limits[B] *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. 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		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y		N	
Dissolution (%LC) (Corealis-28602-8-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline Time (min.)	%LC	Range	%LC	Range	%LC[F]	Range[F]
	10	30	11-53	39	28-56	26	5-58
	20	87	79-98	95	81-102	85	65-103
	(Q=80%) 30	101	99-103	103	99-106	97	90-104
	45	104	103-105	104	103-106	100	95-104
	Trospium Chloride Time (min.)	%LC	Range	%LC	Range	%LC[F]	Range[F]
	10	26	12-47	36	19-48	24	3-51
	20	84	74-91	91	80-99	83	64-102
	(Q=80%) 30	98	93-103	98	94-104	94	84-103
	45	102	95-105	99	95-105	97	89-104
	Method Revision	01		01		01	
Microbial Limits [E] 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. 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-AO-01)	Unspecified impurity (RRT 0.23)	0.14	0.14	0.14
	Unspecified impurity (RRT 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-AO-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-AO)	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)[4] (Corealis-28602-AO)	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-D)	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 [5] 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		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y		Y	
Dissolution (%LC) (Corealis-29602-8-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline Time (min.)	%LC	Range	%LC	Range	%LC	Range
	10	27	7-69	41	7-94	26	10-48
	20	86	74-99	98	94-105	95	89-101
	(Q=80%) 30	98	86-104	103	101-105	105	105-107
	45	101	91-105	103	102-105	106	105-108
	Trospium Chloride Time (min.)	%LC	Range	%LC	Range	%LC	Range
	10	26	7-65	36	5-82	22	9-39
	20	84	75-93	92	86-97	91	87-93
	(Q=80%) 30	96	89-101	96	92-100	100	97-103
	45	99	93-102	96	93-100	101	97-104
	Method Revision	01		01		01	
Microbial Limits[8] 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. 33

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) (Corsaks-29802-8-01) (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	88	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	91	77-85
	(Q=80%) 30	96	89-101	94	92-96
	45	99	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. 34

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	Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y	Y	N
Description *(Visual)*		Off-white opaque hard shell capsule with no markings	No change as compared to initials	No change as compared to initials
Water content by KF *(USP <921>, Method 1a) (n=3)*	%w/w	2.9	3.1	2.8
Assay *(Coreal/s-28602-AD-01) (n=2)*	% 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	96.4
	mg Trospium Chloride/capsule	18.9	20.3	19.1
	Method Revision	01	02	03
Related substances (%LC)[a] *(Coreal/s-28602-AD-01) (n=2)*	Trospium Chloride related compound B	Not detected	Not detected	Not detected
	Trospium Chloride related compound A	Not detected	<0.1	0.14
	Unspecified impurity (Xanomeline_RRT0.24)[c, d]	0.15	0.14	0.14
	Unspecified impurity (Xanomeline_RRT1.10)[c, d]	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		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) (Coreails-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	27	7-69	41	7-94	28	10-48
	20	86	74-99	98	94-105	95	89-101
	(Q=80%) 30	98	86-104	103	101-105	105	105-107
	45	101	91-105	103	102-105	106	105-108
	Trospium Chloride	%LC	Range	%LC	Range	%LC	Range
	Time (min.)						
	10	26	7-65	35	5-82	22	9-39
	20	84	75-93	92	86-97	91	87-93
	(Q=80%) 30	96	89-101	96	92-100	100	97-103
	45	99	93-102	96	93-100	101	97-104
	Method Revision	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. 36

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) *(Corsair-28602-8-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)*	Xanomeline	%LC	Range	%LC	Range
	Time (min.)				
	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	%LC	Range	%LC	Range
	Time (min.)				
	10	26	7-65	12	5-34
	20	84	75-93	91	77-85
	(Q=80%) 30	96	89-101	94	92-96
	45	99	93-102	97	95-100
	Method Revision	01		01	
Microbial Limits® *USP<61>, <62>*	Total Yeasts and Molds Counts (TYMC): ≤100 clu/g	<50 clu/g		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 clu/g	< 500 clu/g		N/A	
	Escherichia coli: Absent	Absent		N/A	

FIG. 37

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		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y		N	
Dissolution (%LC) *(Corealis-28802-8-01)* *(n=6)* *(900 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	93-108	99	94-103
	Method Revision	01		01		01	
Microbial Limits[a] *USP<61>, <62>*	Total Yeasts and Molds Counts (TYMC): ≤100 clu/g	<50 clu/g		N/A		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 clu/g	< 500 clu/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) (Corealis-28602-AO-01)	Unspecified impurity (RRT 0.23)	0.14	0.14	0.14
	Unspecified impurity (RRT 1.08)	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) (Corealis-28602-AO-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) (Corealis-28602-AO)	Xanomeline: 90 - 110% label claim (68 – 83 mg Xanomeline/capsule)
	Trospium Chloride: 90 - 110% label claim (18 – 22mg Trospium Chloride/capsule)
Related Substances (%LC)* (Corealis-28602-AO)	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. 41

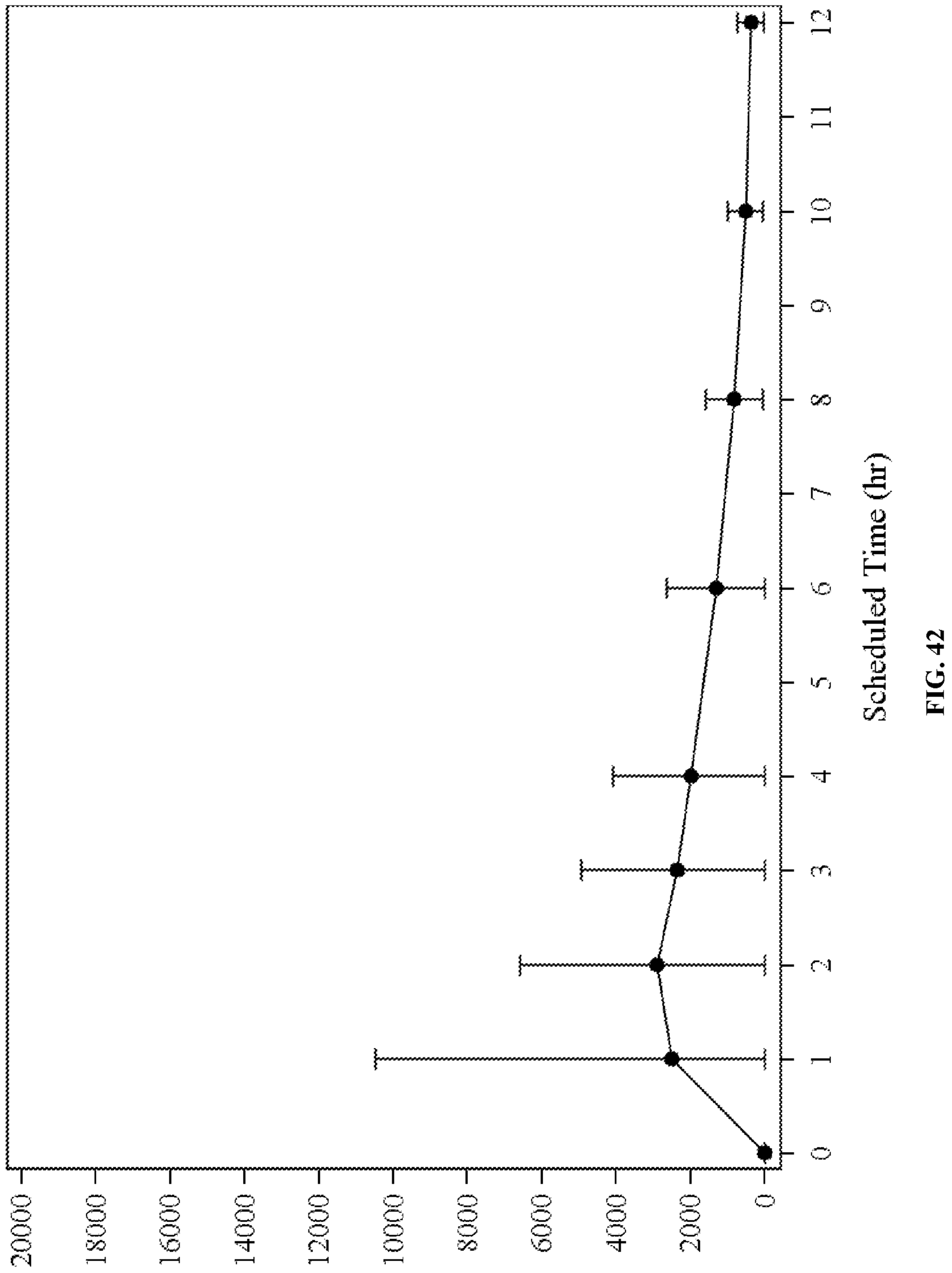
Mean (+/-SD) Xanomeline (pg/mL)
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
Scheduled Time (hr)
0
1
2
3
4
5
6
7
8
9
10
11
12

FIG. 42

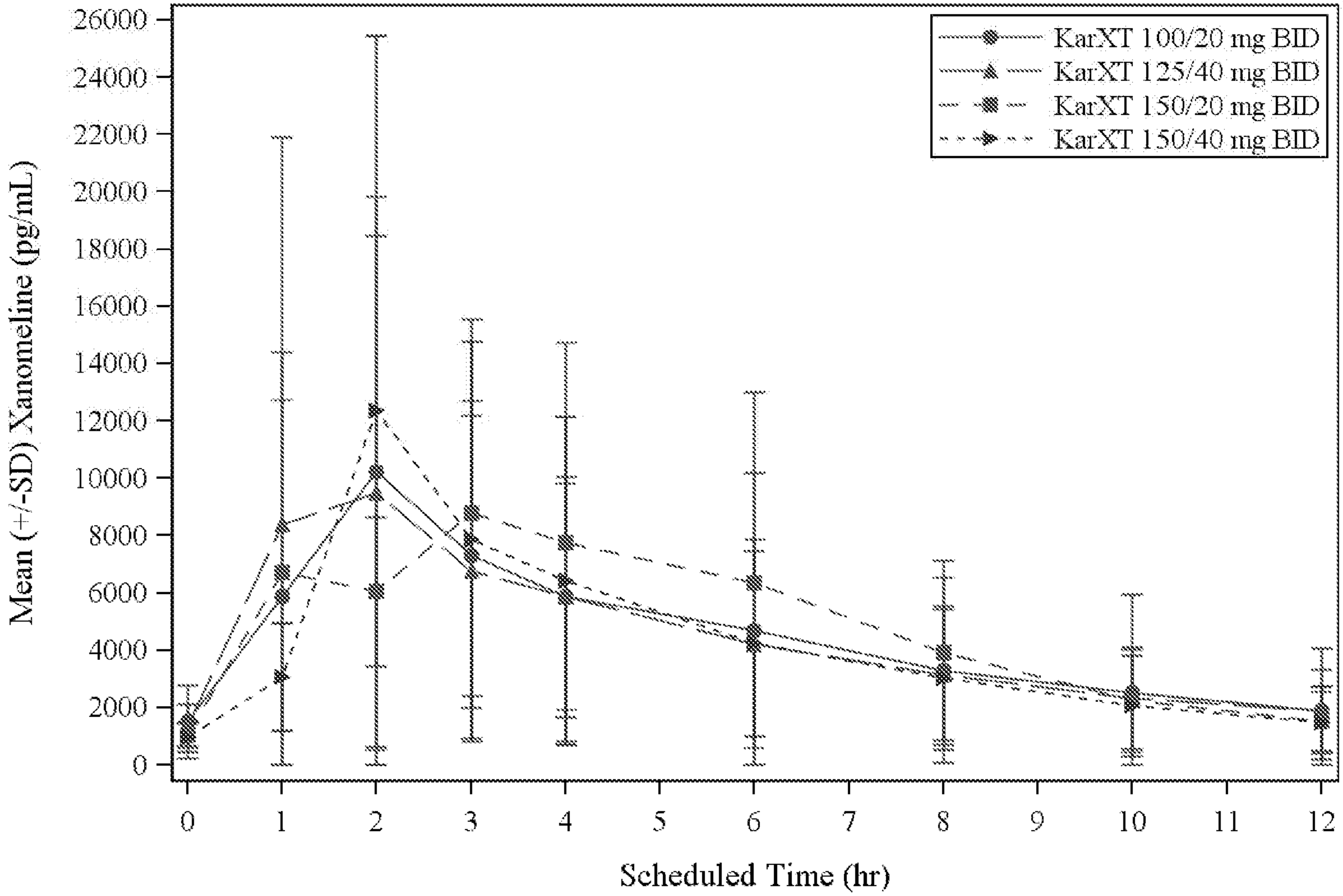
KarXT 100/20 mg BID
KarXT 125/40 mg BID
KarXT 150/20 mg BID
KarXT 150/40 mg BID
Mean (+/-SD) Xanomeline (pg/mL)
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
0
1
2
3
4
5
6
7
8
9
10
11
12
Scheduled Time (hr)

FIG. 43

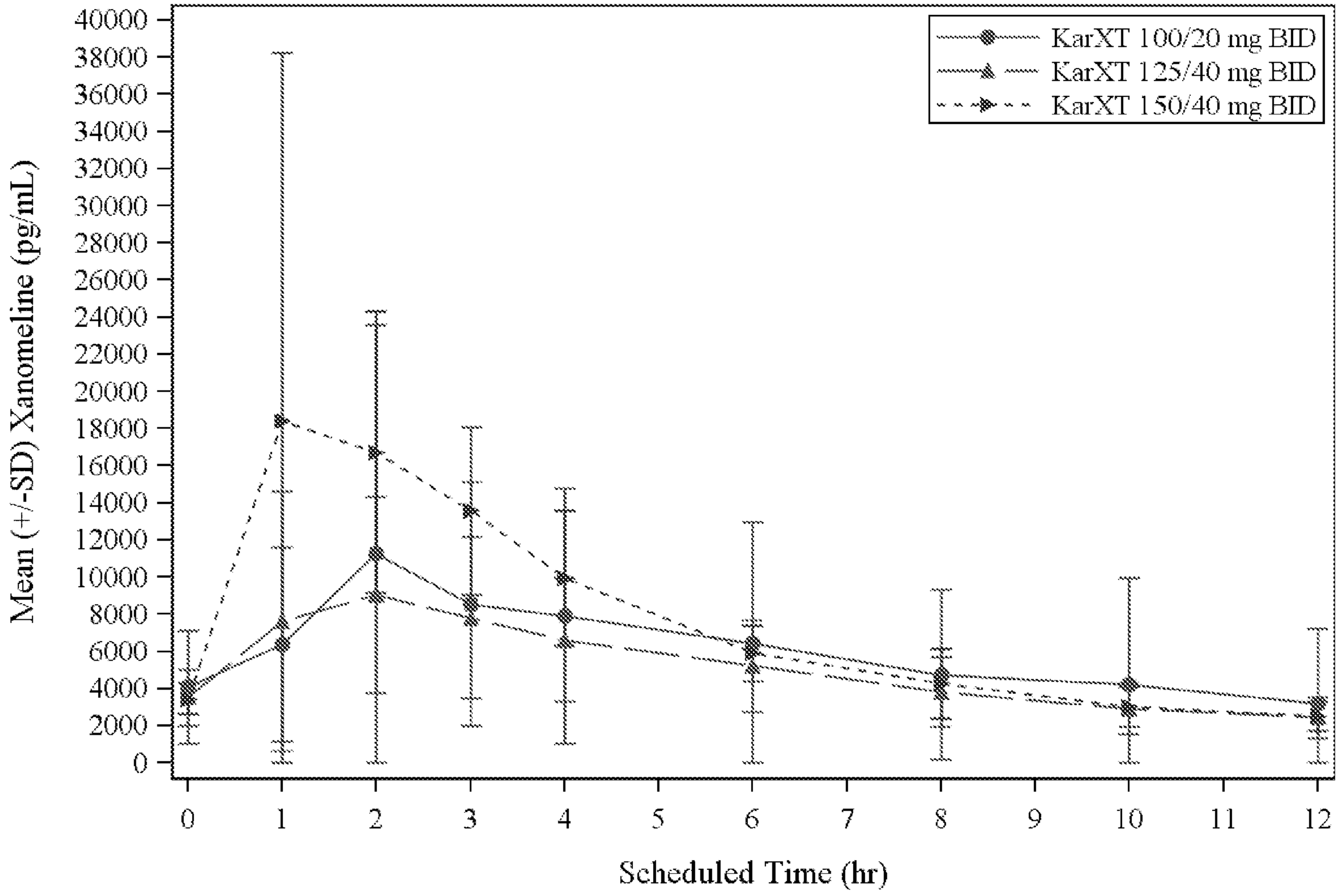
KarXT 100/20 mg BID
KarXT 125/40 mg BID
KarXT 150/40 mg BID
Mean (+/-SD) Xanomeline (pg/mL)
40000
38000
36000
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
0
1
2
3
4
5
6
7
8
9
10
11
12
Scheduled Time (hr)

FIG. 44

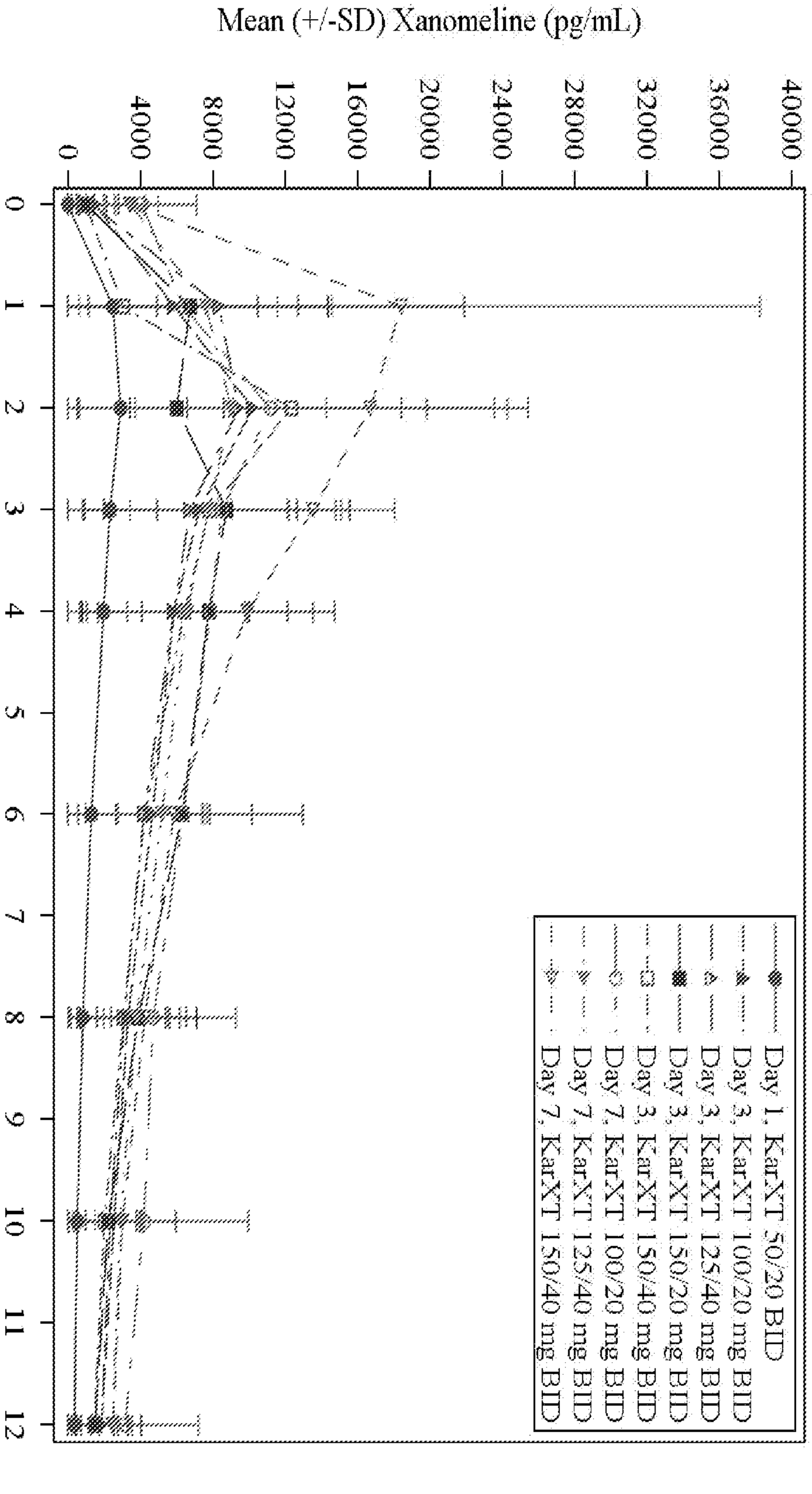
Mean (+/-SD) Xanomeline (pg/mL)
0
4000
8000
12000
16000
20000
24000
28000
32000
36000
40000
Scheduled Time (hr)
0
1
2
3
4
5
6
7
8
9
10
11
12
Day 1, KarXT 50/20 BID
Day 3, KarXT 100/20 mg BID
Day 3, KarXT 125/40 mg BID
Day 3, KarXT 150/20 mg BID
Day 3, KarXT 150/40 mg BID
Day 7, KarXT 100/20 mg BID
Day 7, KarXT 125/40 mg BID
Day 7, KarXT 150/40 mg BID

FIG. 45

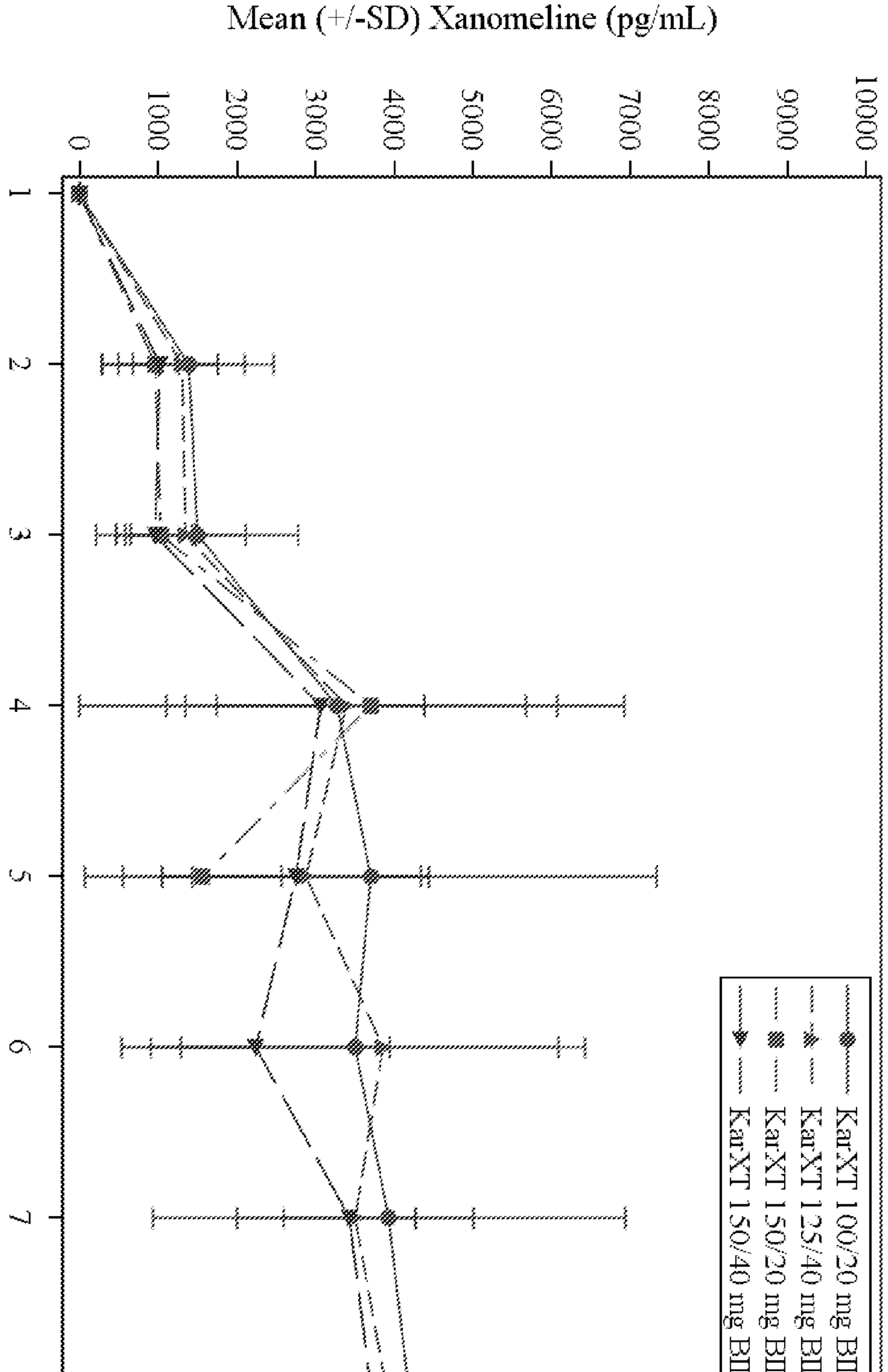
Mean (+/-SD) Xanomeline (pg/mL)
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000
1
2
3
4
5
6
7
8
Actual Study Day
KarXT 100/20 mg BID
KarXT 125/40 mg BID
KarXT 150/20 mg BID
KarXT 150/40 mg BID

FIG. 46

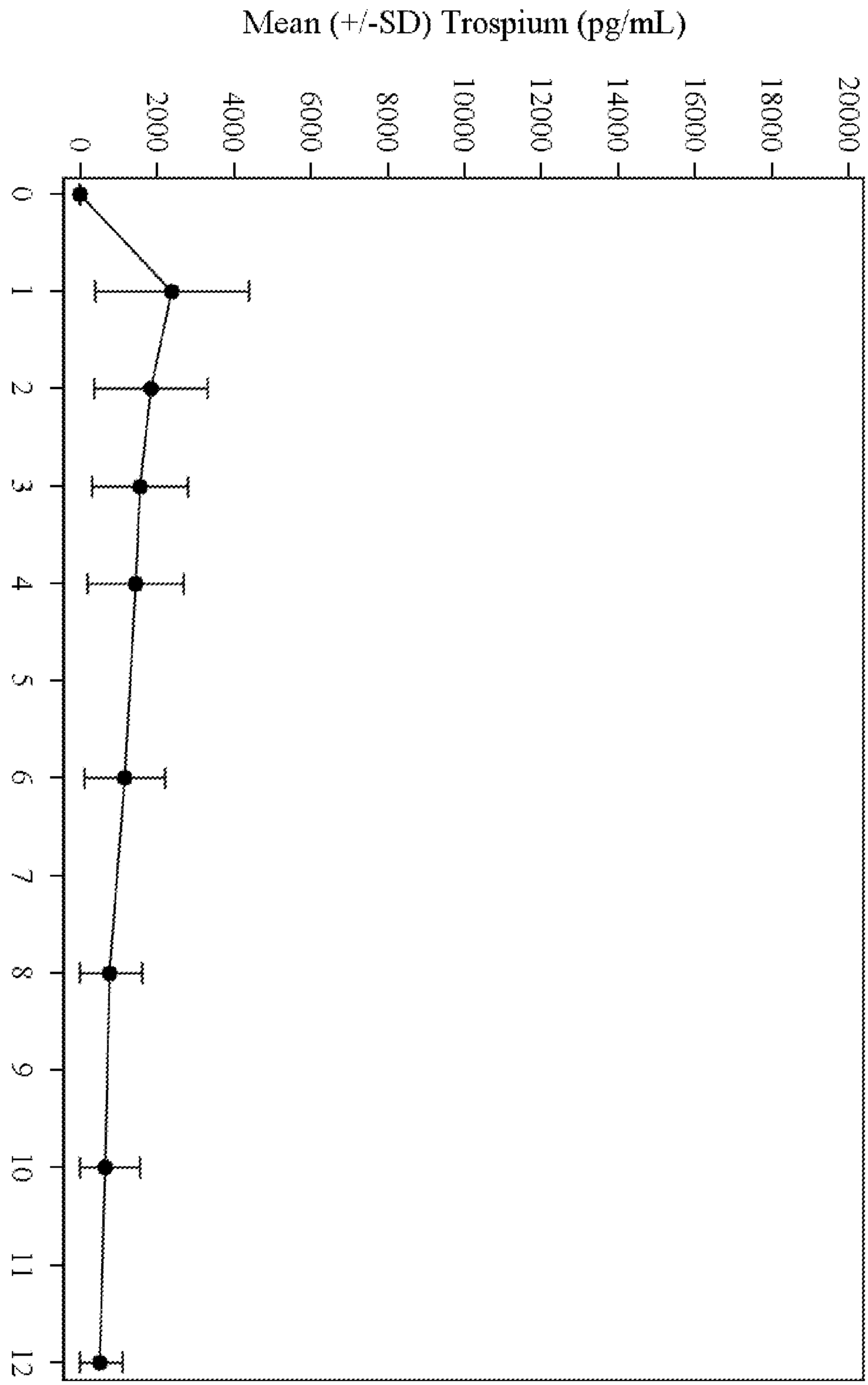
Mean (+/-SD) Trospium (pg/mL)
0
2000
4000
6000
8000
10000
12000
14000
16000
18000
20000
0
1
2
3
4
5
6
7
8
9
10
11
12
Scheduled Time (hr)

FIG. 47

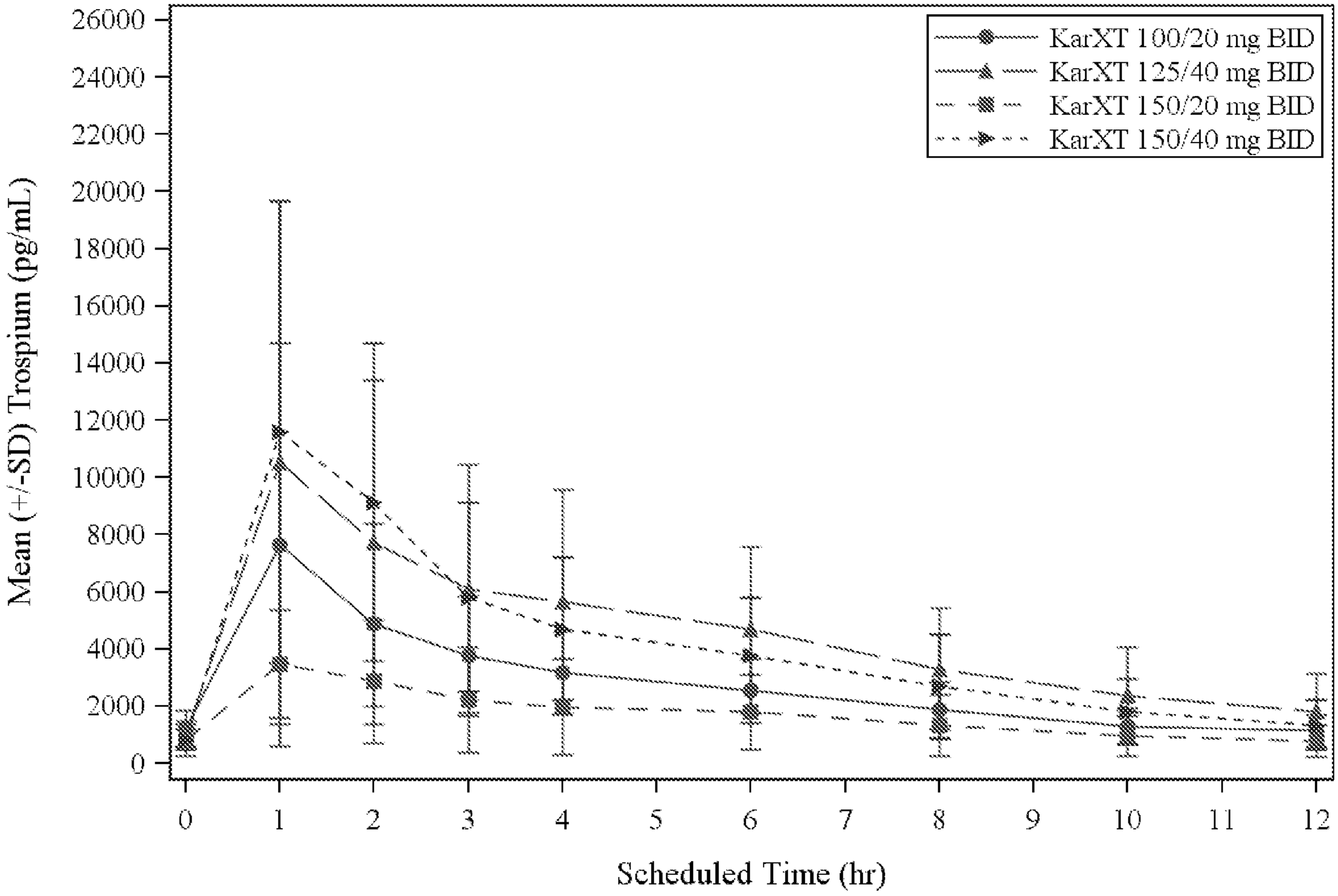
KarXT 100/20 mg BID
KarXT 125/40 mg BID
KarXT 150/20 mg BID
KarXT 150/40 mg BID
Mean (+/-SD) Trospium (pg/mL)
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
0
1
2
3
4
5
6
7
8
9
10
11
12
Scheduled Time (hr)

FIG. 48

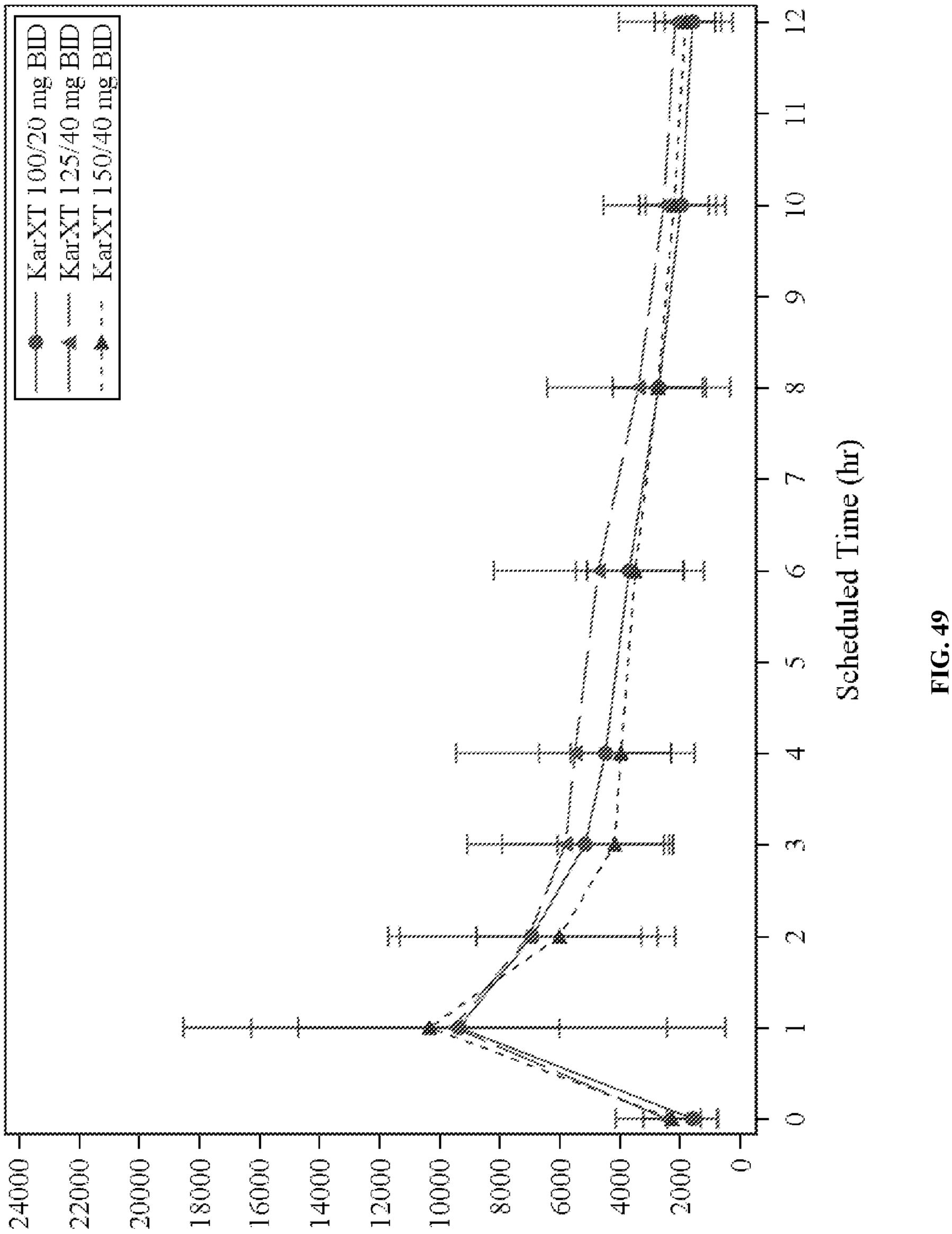
KarXT 100/20 mg BID
KarXT 125/40 mg BID
KarXT 150/40 mg BID
Scheduled Time (hr)
Mean (+/-SD) Trospium (pg/mL)
0
1
2
3
4
5
6
7
8
9
10
11
12
2000
4000
6000
8000
10000
12000
14000
16000
18000
20000
22000
24000

FIG. 49

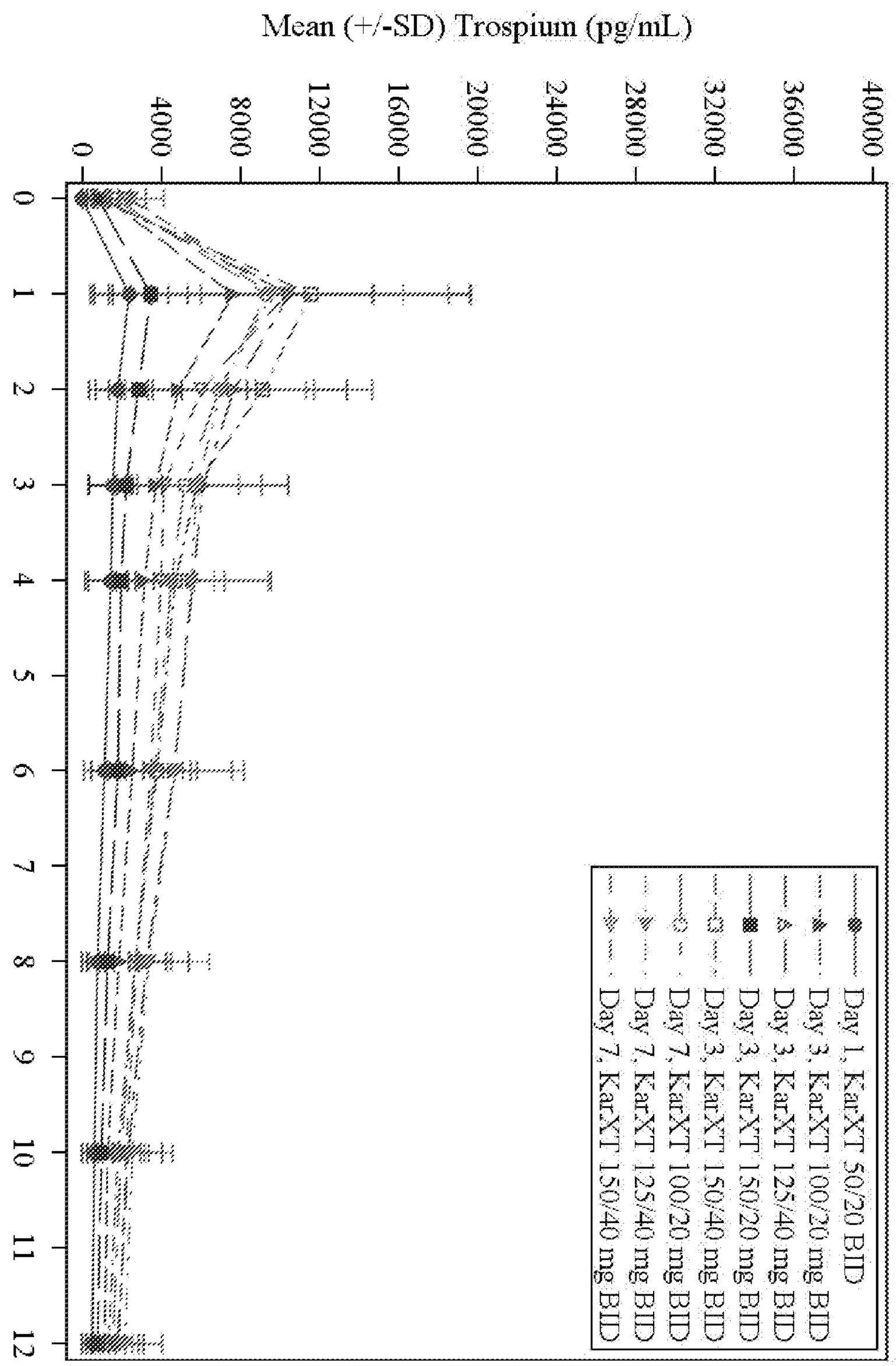
Mean (+/-SD) Trospium (pg/mL)
0
4000
8000
12000
16000
20000
24000
28000
32000
36000
40000
0
1
2
3
4
5
6
7
8
9
10
11
12
Scheduled Time (hr)
Day 1, KarXT 50/20 BID
Day 3, KarXT 100/20 mg BID
Day 3, KarXT 125/40 mg BID
Day 3, KarXT 150/20 mg BID
Day 3, KarXT 150/40 mg BID
Day 7, KarXT 100/20 mg BID
Day 7, KarXT 125/40 mg BID
Day 7, KarXT 150/40 mg BID

FIG. 50

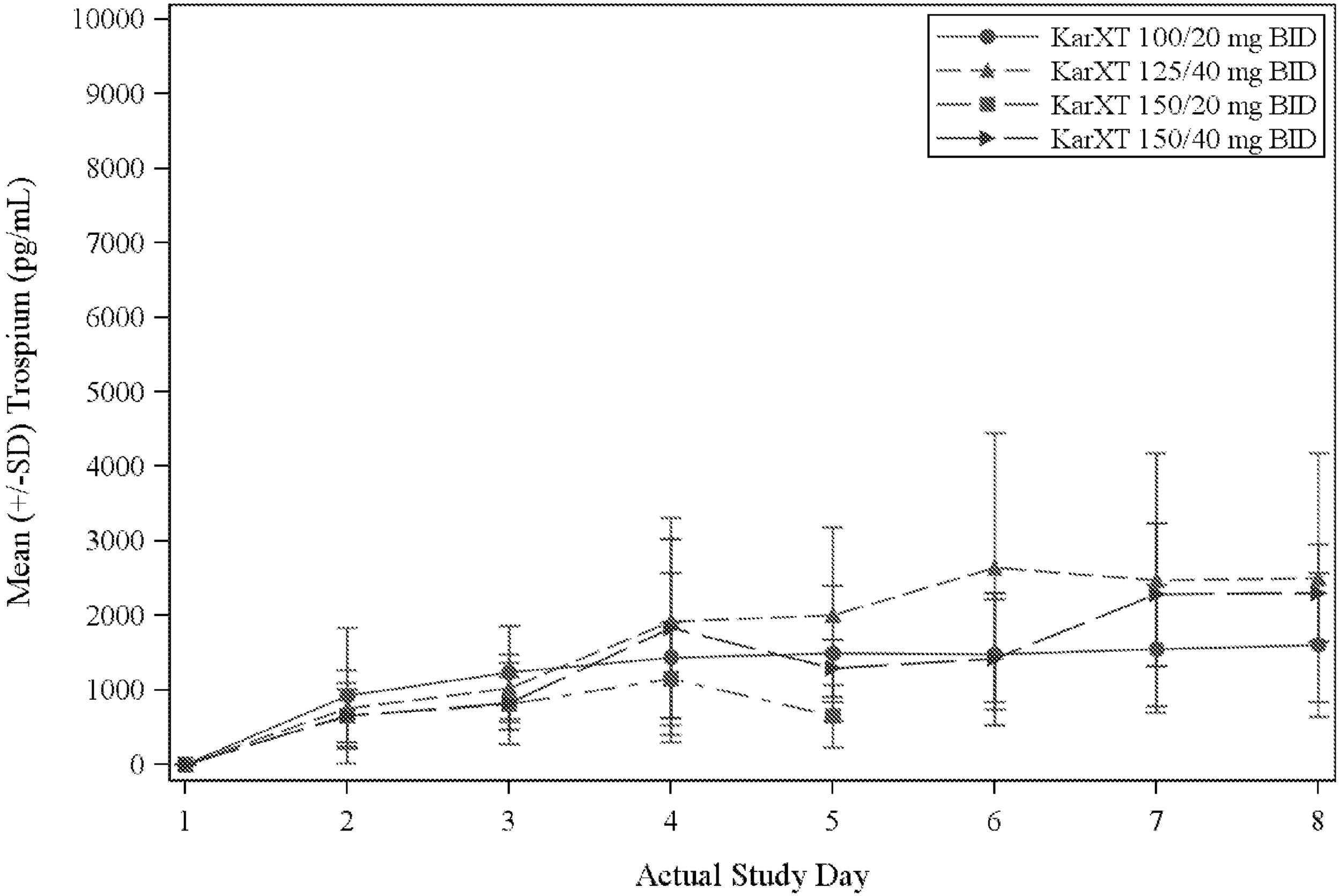
KarXT 100/20 mg BID
KarXT 125/40 mg BID
KarXT 150/20 mg BID
KarXT 150/40 mg BID
Mean (+/-SD) Trospium (pg/mL)
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
1
2
3
4
5
6
7
8
Actual Study Day

FIG. 51