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Supplementary Material

Article Title: Brexpiprazole in Combination with Sertraline and as Monotherapy in Posttraumatic Stress Disorder: A Full-Factorial Randomized Clinical Trial

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LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

DISCLAIMER

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eMethods. Statistical Analysis

Efficacy was analyzed in a modified intention-to-treat sample, comprising all randomized participants who took at least one dose of trial drug, and had a randomization (Week 1) and at least one post-randomization CAPS-5 total score measurement. All continuous efficacy endpoints, including the primary endpoint, were analyzed using separate MMRMs, with an unstructured variance–covariance structure and with score change from randomization (Week 1) as the dependent variable. The model for the fixed effects included terms of treatment, site, type of trauma (combat-related: yes/no), visit, an interaction term of treatment by visit, and the interaction term of Week 1 score by visit as a covariate. Small sites that did not have ≥1 evaluable participant in each treatment arm and each type of trauma (combat-related: yes/no) in Period B were pooled to form collected sites for the purpose of analysis. The model included all scheduled visits from Week 1 to Week 12. The contrast (i.e., least squares mean difference between specified pairs of treatment groups) at the Week 10 visit was estimated from the interaction term and served as the primary treatment comparison. The point estimate and 95% confidence interval estimate of the contrast at Week 10 are reported. CAPS-5 response was analyzed in a last observation carried forward dataset using the Cochran–Mantel–Haenszel general association test controlling for trial center and type of trauma (combat-related: yes/no).

A planned sample size of 68 participants per arm was estimated to achieve 80% power at a two-sided alpha level of 0.05 to detect a treatment difference of -6.5 points (standard deviation, 13) in CAPS-5 total score change from randomization (Week 1) to Week 10. Adjusting for 10% non-evaluable participants, the total number of participants to be randomized was 75 per arm. Further adjusting for 10% dropout between baseline and randomization, approximately 332 participants were planned to be enrolled in the trial.

A hierarchical testing procedure that was planned in the protocol was removed from the final statistical analysis plan and not performed.

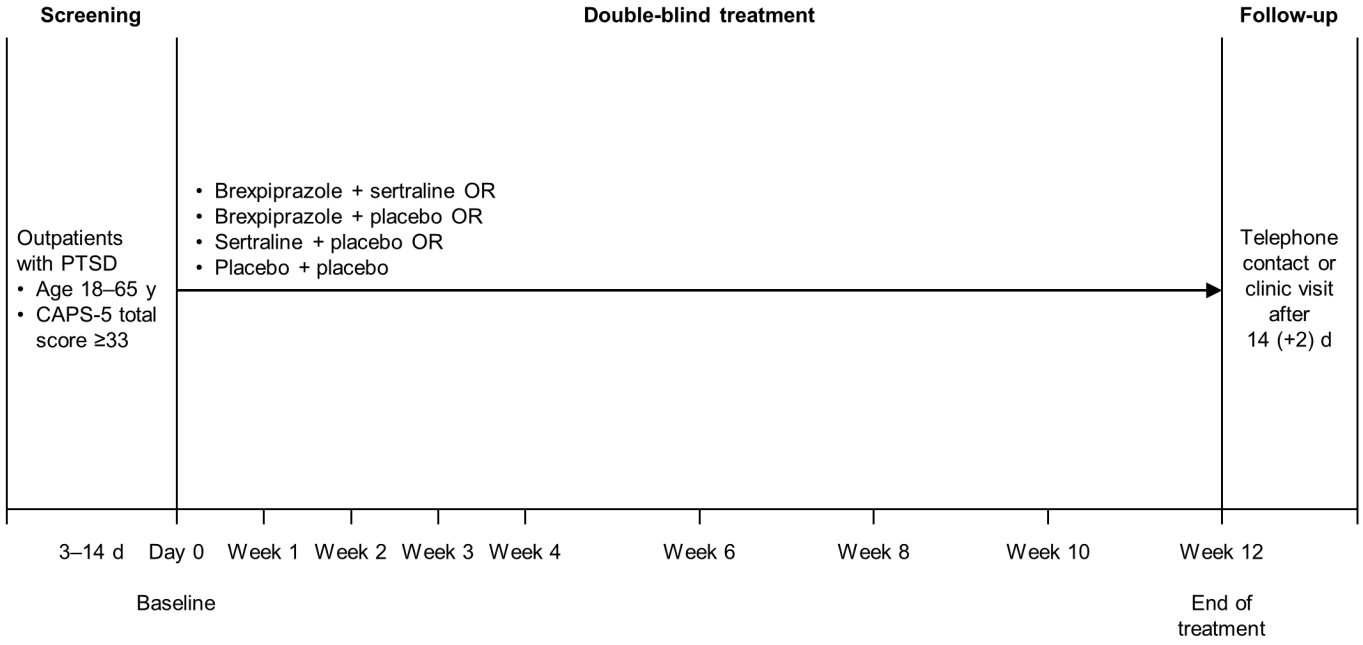
In Period A, CAPS-5 total score change is presented using descriptive statistics.

Safety was analyzed in a sample comprising all randomized participants who took at least one dose of trial drug. Safety results are presented using descriptive statistics.

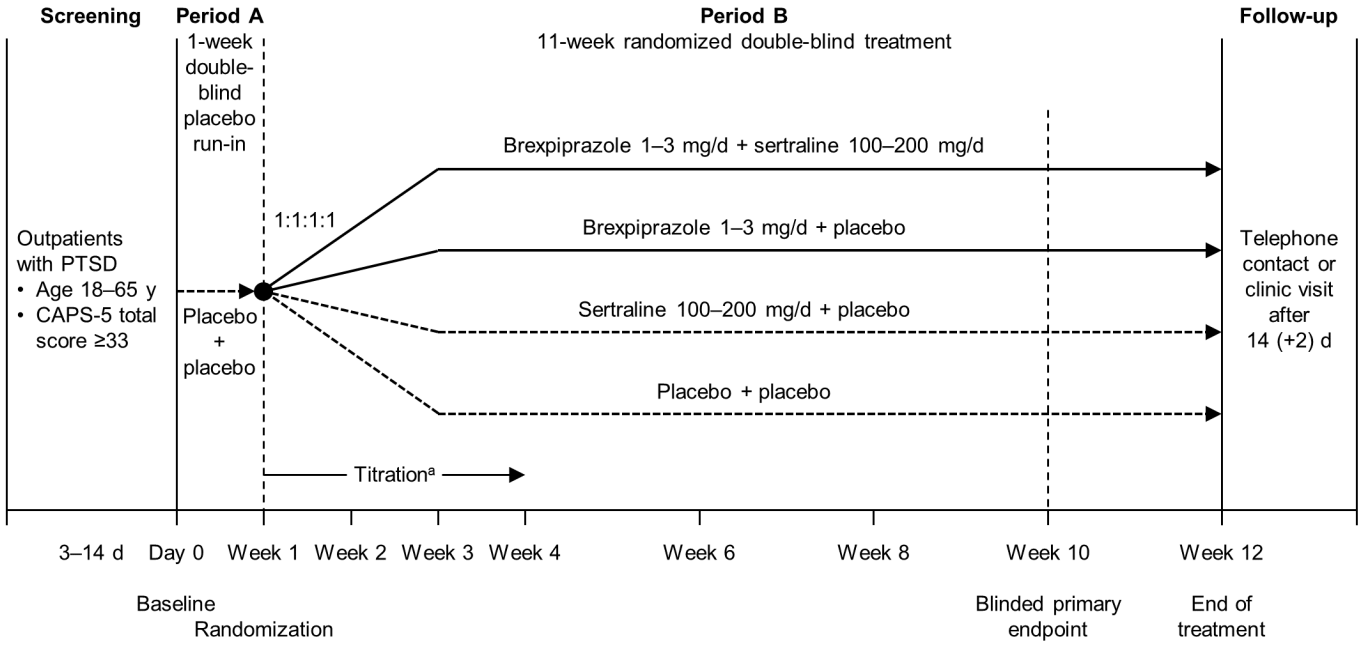
All analyses were performed using SAS version 9.4 (SAS Institute Inc; Cary, NC).

Supplementary Figure 1. Trial Design

A. Blinded design



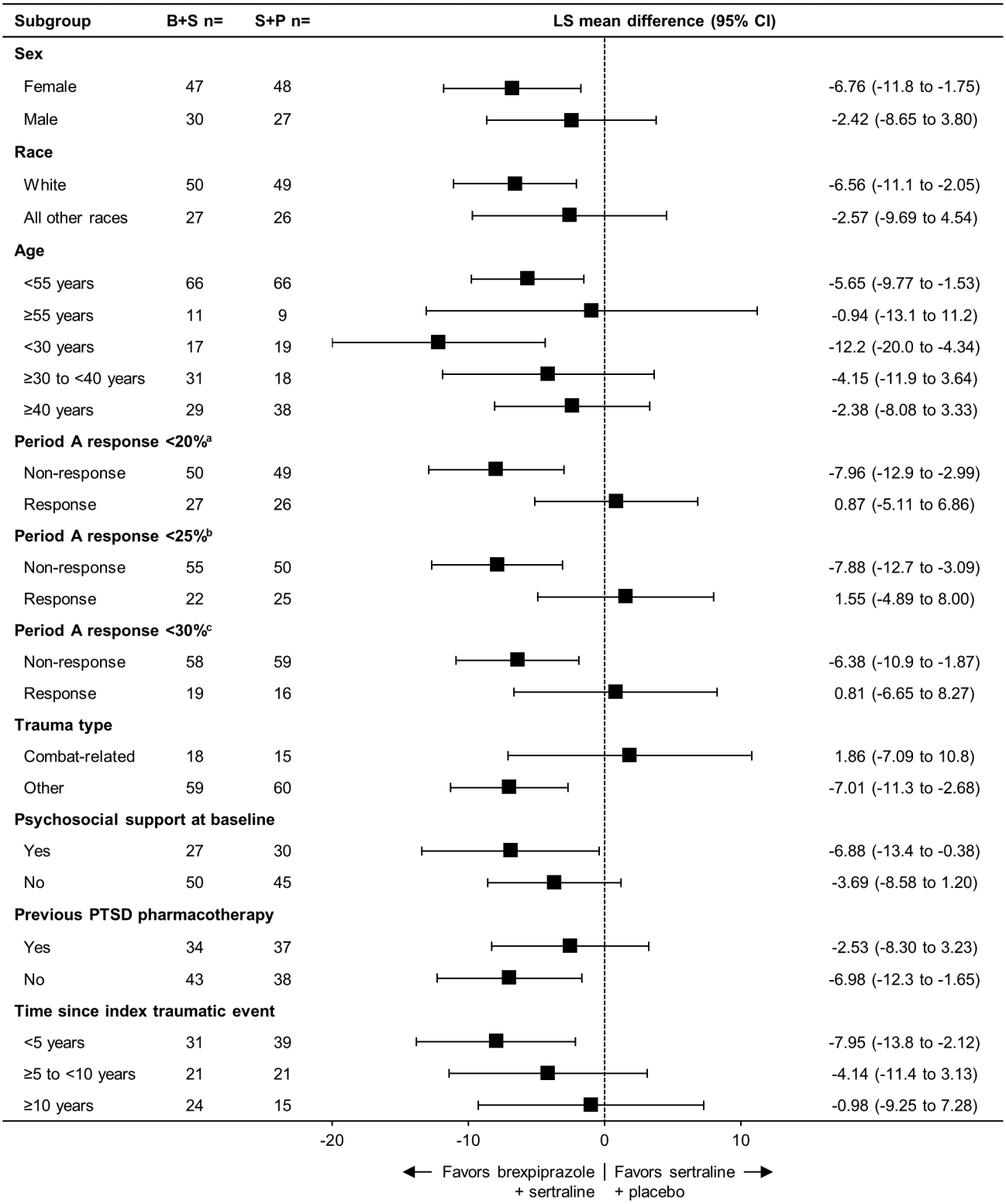
B. Unblinded design



[a]Brexpiprazole: Week 1, 0.5 mg/d; Week 2, 1 mg/d; Week 3, 2 mg/d. At Week 4, based on efficacy and tolerability, options were to stay at 2 mg/d, increase to 3 mg/d, or decrease to 1 mg/d. Dose decreases (to a minimum of 1 mg/d) were permitted until Week 6. Sertraline: Week 1, 50 mg/d; Week 2, 100 mg/d; Week 3, 150 mg/d. At Week 4, based on efficacy and tolerability, options were to stay at 150 mg/d, increase to 200 mg/d, or decrease to 100 mg/d. Dose decreases (to a minimum of 100 mg/d) were permitted until Week 6. Participants in the brexpiprazole + sertraline arm who required a dose increase/decrease had the doses changed for both drugs.

Abbreviations: CAPS-5=Clinician-Administered PTSD Scale for DSM-5; PTSD=post-traumatic stress disorder.

Supplementary Figure 2. Change in CAPS-5 Total Score From Randomization (Week 1) to Week 10 by Subgroup, For Brexpiprazole + Sertraline Vs Sertraline + Placebo (Efficacy Sample)



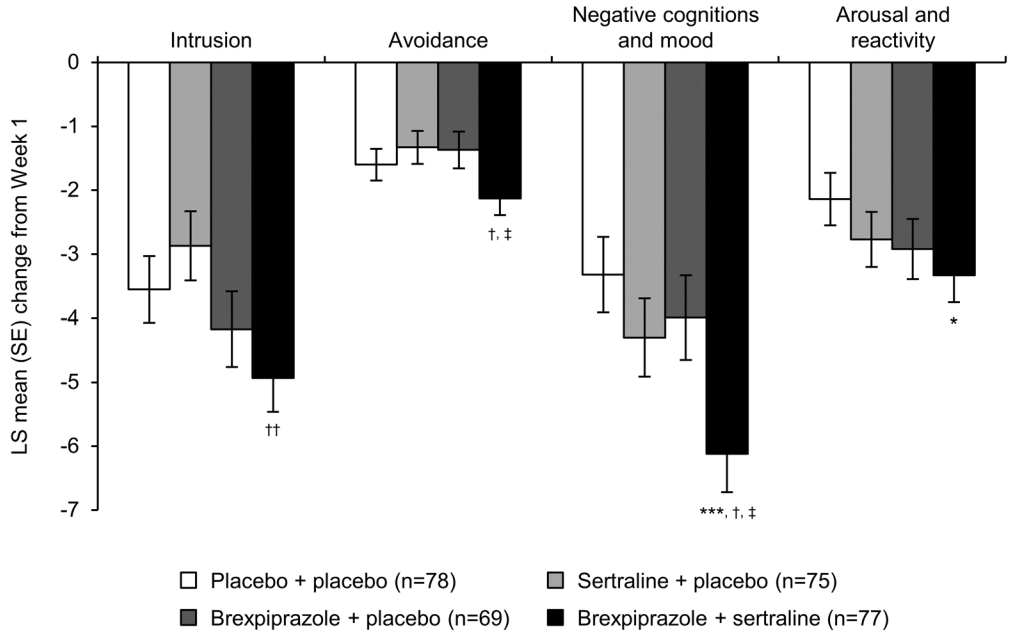
[a]<20% improvement during Period A (placebo run-in) and CAPS-5 total score ≥27 at randomization (Week 1).

[b]<25% improvement during Period A (placebo run-in) and CAPS-5 total score ≥27 at randomization (Week 1).

[c]<30% improvement during Period A (placebo run-in) and CAPS-5 total score ≥27 at randomization (Week 1).

Abbreviations: B+S=brexpiprazole + sertraline; CAPS-5=Clinician-Administered PTSD Scale for DSM-5; PTSD=post-traumatic stress disorder; S+P=sertraline + placebo. N-values are for participants with measurements at randomization (Week 1).

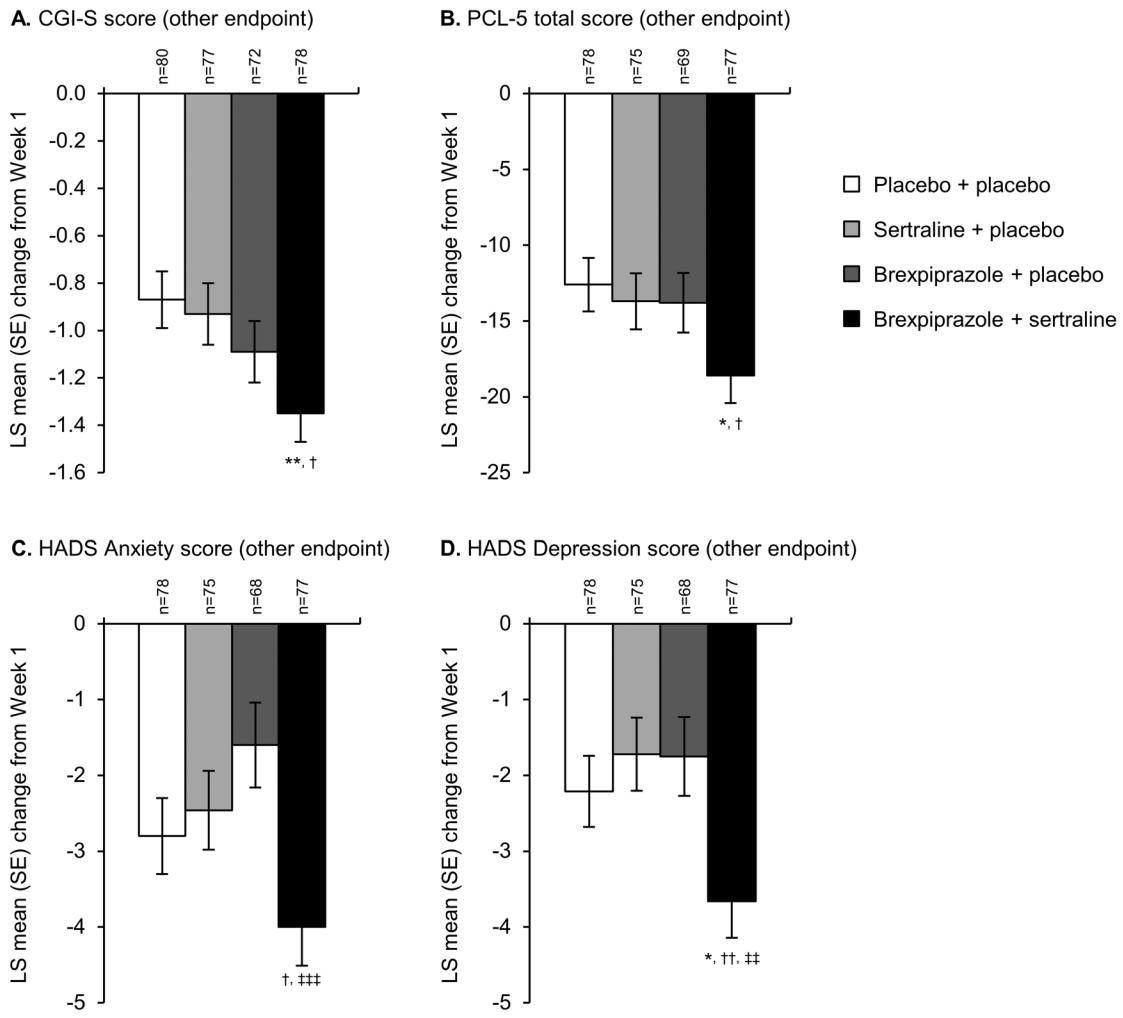
Supplementary Figure 3. Change in CAPS-5 Symptom Cluster Scores From Randomization (Week 1) to Week 10



*P<.05, ***P<.001 vs placebo + placebo; †P<.05, ††P<.01 vs sertraline + placebo; ‡P<.05 vs brexpiprazole + placebo (nominal P values with no adjustment for multiplicity); mixed model for repeated measures; efficacy sample.

Abbreviations: CAPS-5=Clinician-Administered PTSD Scale for DSM-5; PTSD=post-traumatic stress disorder. N-values are for participants with measurements at randomization (Week 1).

Supplementary Figure 4. Change in CGI-S, PCL-5 Total, HADS Anxiety, and HADS Depression Scores From Randomization (Week 1) to Week 10



*P<.05, **P<.01 vs placebo + placebo; †P<.05, ††P<.01 vs sertraline + placebo; ‡‡P<.01, ‡‡‡P=.001 vs brexpiprazole + placebo (nominal P values with no adjustment for multiplicity); mixed model for repeated measures; efficacy sample.

Abbreviations: CGI-S=Clinical Global Impression – Severity of illness; HADS=Hospital Anxiety and Depression Scale; PCL-5=PTSD Checklist for DSM-5; PTSD=post-traumatic stress disorder. N-values are for participants with measurements at randomization (Week 1).

Supplementary Table 1. List of Principal Investigators and Trial Sites

Site #	Principal Investigator Name	Address	# Screened	# Enrolled	# Discon-tinued
001	Sarah D Atkinson	Finger Lakes Clinical Research, 885 South Winton Road, Rochester, NY 14618-1609	14	11	3
002	Michael D Banov	Northwest Behavioral Research Center, 11755 Pointe Pl, Suite A-1, Roswell, GA 30076-4657	15	11	4
003	Ronald Loewy Brenner	Neurobehavioral Research, Inc., 74 Carman Avenue, Cedarhurst, NY 11516	23	14	3
004	Armen K Goenjian	Collaborative Neuroscience Network, Inc, 19401 S. Vermont Ave, Suite F-100, Torrance, CA 90502-4432	19	8	0
005	Lee Ann Kelley	Noesis Pharma Research, 16601 N 40th St, Suite 101, Phoenix, AZ 85032	3	1	0
006	Louise M Thurman	IPS Research Company, 1111 North Lee Avenue, Suite 400, Oklahoma City, OK 73103	31	3	1
007	Benny L Barnhart	Grayline Clinical Drug Trials, 3300 Seymour Highway, Wichita Falls, TX 76309	16	9	1
008	David Purselle	iResearch Atlanta, LLC, 125 Clairemont Avenue, Suite 470, Decatur, GA 30030	25	11	6
009	Howard R Hassman	Hassman Research Institute, 175 Cross Keys Rd, Bldg 300B, Berlin, NJ 08009	12	8	2
010	Rishi Kakar	Innovative Clinical Research, Inc., 7481 W Oakland Park Blvd, Suite 205, Lauderhill, FL 33319	11	4	1
013	Vishaal Mehra	Artemis Institute for Clinical Research, LLC, 770 Washington St, Suite 300, San Diego, CA 92103	19	7	2
014	Sejal Patel	Compass Research North, LLC, 100 West Gore Street, Suite 202, Orlando, FL 32806	10	4	1
016	James J Whalen	Lincoln Research, 640 George Washington Hwy, Bldg C, Suite 202, Lincoln, RI 02865-4207	5	1	0
017	Sherry A Soefje	Excell Research, Inc., 3998 Vista Way, Suite 100, Oceanside, CA 92056	22	15	4
018	Nandita Joshi (Jones)	Clinical Neuroscience Solutions, P.A., 5200 Belfort Rd, Suite 420, Jacksonville, FL 32256	18	8	3
019	Anita S Varma	Research Strategies of Memphis, LLC, 5395 Estate Office Park Dr, Suite 2, Memphis, TN 38119	2	1	0
020	Nick G Vatakis	Social Psychiatry Research Institute (SPRI), 3044 Coney Island Ave, Suite 201, Brooklyn, NY 11235	8	6	1

Site #	Principal Investigator Name	Address	# Screened	# Enrolled	# Discon-tinued
021	Kelly Yokum	Olympian Clinical Research, 2919 W Swann Ave, Suite 205, Tampa, FL 33609-4038	10	4	4
022	Daniel Francis Chueh	Neuropsychiatric Research Center of Orange County, 1010 W Chapman Ave, Orange, CA 92868-2847	15	9	3
023	Andrew J Cutler	Meridien Research, 8043 Cooper Creek Blvd, Suite 107, Bradenton, FL 34201-2142	17	4	1
025	Valerie K Arnold	Clinical Neuroscience Solutions, P.A., 1340 Poplar Ave, Suite 420, Memphis, TN 38119	13	5	2
026	Courtney D Nixon	Paradigm Research Professionals, 5400 N Classen Blvd, Suite 110, Oklahoma City, OK 73118	8	4	0
027	Michael Liebowitz	The Medical Research Network, LLC, 134 East 93rd Street, Suite 201A, New York, NY 10128-1704	9	5	1
028	Andrew C Sedillo	MCB Clinical, 110 S Parkside Dr, Colorado Springs, CO 80910	24	12	5
029	Angelo Sambunaris	The Institute for Advance Medical Research, 3015 Flowers Road South, Atlanta, GA 30341	3	2	2
030	Beal G Essink	Oregon Center for Clinical Investigations, Inc., 905 SE 14th Ave, Portland, OR 97214	20	15	4
031	Drissana Tran	Oregon Center for Clinical Investigations, Inc., 702 Church St. NE, Salem, OR 97301-2404	27	22	3
032	Diane M Highum	CiTrials, 17800 Woodruff Ave, Suite B, Bellflower, CA 90706	54	32	6
033	Robert Molpus	Clinical Neuroscience Solutions, P.A., Dba CNS Healthcare, 618 E South St, Suite 100, Orlando, FL32801-2987	23	11	2
034	Don Anderson	Anderson Clinical Research, 2068 Orange Tree Lane, Suite 226, Redlands, CA 92374	5	5	1
035	Jeffrey Apter	Global Medical Institute, LLC, Woodlands Professional Building, 256 Bunn Dr, Suite 6, Princeton, CA 08540	19	11	3
036	Jim G Aukstuolis	Woodland International Research Group, 910 Autumn Road, Suite 3, Little Rock, AR 72211	13	4	0
037	Daniel Gruener	St. Louis Clinical Trials LLC, 10330 Old Olive Road, St. Louis, MO 63118	6	2	0
038	Jelena A Kunovac	Altea Research Institute, 3012 W Charleston Blvd, Suite 100, Las Vegas, NV 89102-1972	35	16	5
039	Fayz Hudefi	Woodland Research Northwest, LLC, 609 E Dyke Rd, Rogers, AZ 72758-0132	17	8	4

Site #	Principal Investigator Name	Address	# Screened	# Enrolled	# Discon-tinued
040	Jesse M Carr	Behavioral Research Specialists, LLC, 230 N. Maryland Avenue, Suite 207, Glendale, CA 91206	14	8	1
041	Stacey Layle	Artemis Institute for Clinical Research, LLC, 365 S Rancho Santa Fe Rd, Suite 202, San Marcos, CA 92078-2338	6	2	1
042	Richard Weisler	Richard H. Weisler, MD, PA, 700 Spring Forest Rd, Suite 125, Raleigh, NC 27609-9148	19	8	0
043	Jason Clay Miller	Clinical Trials of Texas, Inc., 7940 Floyd Curl Drive, Suite 700, San Antonio, TX 78229	15	2	0
045	Steven Szabo	Duke University Medical Center, 40 Duke Medicine Circle, Durham, NC 27710	5	2	0
046	Patricia Pilkinton	Tuscaloosa VA Medical Center, 3701 Loop Rd, Tuscaloosa, AL 35404-5015	5	1	1
051	Zaheer Aslam	Gulf Coast Clinical Research Center, 6150 Diamon Centre Court, Suite 500, Fort Myers, FL 33912	6	6	1
052	James Alan Knutson	Management Core Clinical Research, 2918 Colby Avenue, Suite 101, Everett, WA 98201	14	6	5
053	Brock H Summers	Southern California Research, LLC, 436 N. Roxbury Dr, Suite 222, Beverly Hills, CA 90210	3	2	1
054	Paul E Wylie	Preferred Research Partners, 11219 Financial Centre Pkwy, Suite 320, Little Rock, AR 72211-3800	3	2	1
055	Shivkumar Hatti	Suburban Research Associates, 107 Chesley Drive, Unit 4, Media, PA 19063	4	2	1
057	Gerald Maguire	CITrials, Inc. – Riverside & San Bernardino County, 5700 Division Street, Suite 101, Riverside, CA 92506	2	1	0

Supplementary Table 2. CAPS-5 Total Score Sensitivity Analysis – MNAR Using Pattern Mixture Model With Multiple Imputation – Assume All Dropouts as MNAR (Efficacy Sample)

Shifted from the MAR[a]	Treatment difference		
	Comparison	Difference (95% CI)[b]	*P* value[b]
0	Brex + sert vs placebo + placebo	-6.32 (-10.0 to -2.61)	.001
	Brex + sert vs sert + placebo	-5.46 (-9.26 to -1.67)	.005
	Brex + sert vs brex + placebo	-4.55 (-8.49 to -0.607)	.02
	Brex + placebo vs placebo + placebo	-1.78 (-5.71 to 2.16)	.38
	Sert + placebo vs placebo + placebo	-0.861 (-4.69 to 2.96)	.66
0.65	Brex + sert vs placebo + placebo	-6.19 (-9.91 to -2.47)	.001
	Brex + sert vs sert + placebo	-5.33 (-9.13 to -1.54)	.006
	Brex + sert vs brex + placebo	-4.41 (-8.35 to -0.472)	.03
	Brex + placebo vs placebo + placebo	-1.78 (-5.71 to 2.15)	.37
	Sert + placebo vs placebo + placebo	-0.858 (-4.68 to 2.97)	.66
1.3	Brex + sert vs placebo + placebo	-6.06 (-9.77 to -2.34)	.001
	Brex + sert vs sert + placebo	-5.20 (-8.99 to -1.41)	.007
	Brex + sert vs brex + placebo	-4.27 (-8.21 to -0.336)	.03
	Brex + placebo vs placebo + placebo	-1.78 (-5.71 to 2.15)	.37
	Sert + placebo vs placebo + placebo	-0.855 (-4.68 to 2.97)	.66
1.95	Brex + sert vs placebo + placebo	-5.92 (-9.64 to -2.21)	.002
	Brex + sert vs sert + placebo	-5.07 (-8.86 to -1.28)	.009
	Brex + sert vs brex + placebo	-4.14 (-8.08 to -0.200)	.04
	Brex + placebo vs placebo + placebo	-1.78 (-5.71 to 2.15)	.37
	Sert + placebo vs placebo + placebo	-0.852 (-4.67 to 2.97)	.66
2.6	Brex + sert vs placebo + placebo	-5.79 (-9.51 to -2.07)	.002
	Brex + sert vs sert + placebo	-4.94 (-8.73 to -1.15)	.01
	Brex + sert vs brex + placebo	-4.00 (-7.94 to -0.064)	.05
	Brex + placebo vs placebo + placebo	-1.79 (-5.72 to 2.15)	.37
	Sert + placebo vs placebo + placebo	-0.849 (-4.67 to 2.97)	.66
3.25	Brex + sert vs placebo + placebo	-5.65 (-9.37 to -1.94)	.003
	Brex + sert vs sert + placebo	-4.81 (-8.60 to -1.01)	.01
	Brex + sert vs brex + placebo	-3.87 (-7.81 to 0.073)	.05
	Brex + placebo vs placebo + placebo	-1.79 (-5.72 to 2.14)	.37
	Sert + placebo vs placebo + placebo	-0.846 (-4.67 to 2.98)	.66
3.9	Brex + sert vs placebo + placebo	-5.52 (-9.24 to -1.80)	.004

Shifted from the MAR[a]	Treatment difference		
	Comparison	Difference (95% CI)[b]	*P* value[b]
	Brex + sert vs sert + placebo	-4.68 (-8.47 to -0.883)	.02
	Brex + sert vs brex + placebo	-3.73 (-7.67 to 0.211)	.06
	Brex + placebo vs placebo + placebo	-1.79 (-5.72 to 2.14)	.37
	Sert + placebo vs placebo + placebo	-0.843 (-4.67 to 2.98)	.67
4.55	Brex + sert vs placebo + placebo	-5.39 (-9.11 to -1.67)	.005
	Brex + sert vs sert + placebo	-4.55 (-8.34 to -0.750)	.02
	Brex + sert vs brex + placebo	-3.59 (-7.54 to 0.349)	.07
	Brex + placebo vs placebo + placebo	-1.79 (-5.73 to 2.14)	.37
	Sert + placebo vs placebo + placebo	-0.840 (-4.67 to 2.99)	.67
5.2	Brex + sert vs placebo + placebo	-5.25 (-8.98 to -1.53)	.006
	Brex + sert vs sert + placebo	-4.41 (-8.21 to -0.616)	.02
	Brex + sert vs brex + placebo	-3.46 (-7.40 to 0.487)	.09
	Brex + placebo vs placebo + placebo	-1.79 (-5.73 to 2.14)	.37
	Sert + placebo vs placebo + placebo	-0.837 (-4.67 to 2.99)	.67
5.85	Brex + sert vs placebo + placebo	-5.12 (-8.84 to -1.39)	.007
	Brex + sert vs sert + placebo	-4.28 (-8.08 to -0.483)	.03
	Brex + sert vs brex + placebo	-3.32 (-7.27 to 0.626)	.10
	Brex + placebo vs placebo + placebo	-1.80 (-5.74 to 2.14)	.37
	Sert + placebo vs placebo + placebo	-0.834 (-4.67 to 3.00)	.67
6.5	Brex + sert vs placebo + placebo	-4.98 (-8.71 to -1.25)	.009
	Brex + sert vs sert + placebo	-4.15 (-7.96 to -0.348)	.03
	Brex + sert vs brex + placebo	-3.19 (-7.14 to 0.766)	.11
	Brex + placebo vs placebo + placebo	-1.80 (-5.74 to 2.14)	.37
	Sert + placebo vs placebo + placebo	-0.831 (-4.67 to 3.00)	.67
7.15	Brex + sert vs placebo + placebo	-4.85 (-8.58 to -1.12)	.01
	Brex + sert vs sert + placebo	-4.02 (-7.83 to -0.213)	.04
	Brex + sert vs brex + placebo	-3.05 (-7.00 to 0.906)	.13
	Brex + placebo vs placebo + placebo	-1.80 (-5.75 to 2.15)	.37
	Sert + placebo vs placebo + placebo	-0.828 (-4.67 to 3.01)	.67
7.8	Brex + sert vs placebo + placebo	-4.72 (-8.45 to -0.979)	.01
	Brex + sert vs sert + placebo	-3.89 (-7.70 to -0.078)	.05
	Brex + sert vs brex + placebo	-2.91 (-6.87 to 1.05)	.15
	Brex + placebo vs placebo + placebo	-1.80 (-5.75 to 2.15)	.37
	Sert + placebo vs placebo + placebo	-0.825 (-4.67 to 3.02)	.67

Shifted from the MAR[a]	Treatment difference		
	Comparison	Difference (95% CI)[b]	*P* value[b]
8.45	Brex + sert vs placebo + placebo	-4.58 (-8.32 to -0.840)	.02
	Brex + sert vs sert + placebo	-3.76 (-7.58 to 0.058)	.05
	Brex + sert vs brex + placebo	-2.78 (-6.74 to 1.19)	.17
	Brex + placebo vs placebo + placebo	-1.81 (-5.76 to 2.15)	.37
	Sert + placebo vs placebo + placebo	-0.822 (-4.67 to 3.02)	.68

[a]Analysis departs from MAR assumption by progressively increasing the delta (treatment effect) until the conclusion from the primary analysis is overturned. When delta is 0 the missing data are assumed to be MAR; when delta is >0 the missing data are assumed to be MNAR.

[b]Derived based on 100 imputations.

Abbreviations: CAPS-5=Clinician-Administered PTSD Scale for DSM-5; MAR=missing at random; MNAR=missing not at random.

Supplementary Table 3. Body Weight, Metabolic Parameters, Vital Signs, QT Interval, and Extrapyramidal symptoms (Safety Sample)

Endpoint[a]	Placebo + placebo		Sertraline + placebo		Brexpiprazole + placebo		Brexpiprazole + sertraline	
	Baseline (Day 0)	Change to last visit	Baseline (Day 0)	Change to last visit	Baseline (Day 0)	Change to last visit	Baseline (Day 0)	Change to last visit
Body weight, kg	86.7 (17.7) (n=82)[b]	0.3 (3.4) (n=82)	87.4 (23.2) (n=79)[b]	-0.2 (2.8) (n=79)	83.2 (22.7) (n=75)[b]	0.7 (2.8) (n=75)	85.6 (24.2) (n=80)[b]	1.4 (2.6) (n=80)
BMI, kg/m^2	30.3 (6.1) (n=82)[b]	0.1 (1.2) (n=82)	30.1 (7.5) (n=79)[b]	-0.1 (0.9) (n=79)	29.8 (7.1) (n=75)[b]	0.3 (1.0) (n=75)	30.0 (7.1) (n=80)[b]	0.5 (0.9) (n=80)
Fasting metabolic parameters, mg/dL								
Glucose	90.3 (10.0) (n=79)	0.7 (13.6) (n=71)	90.9 (14.1) (n=79)	1.4 (15.4) (n=70)	91.1 (9.8) (n=74)	1.3 (15.8) (n=62)	92.0 (12.7) (n=80)	-1.7 (15.5) (n=71)
HDL cholesterol	55.9 (14.3) (n=51)	0.9 (11.2) (n=45)	57.1 (17.9) (n=55)	0.5 (9.4) (n=50)	60.0 (18.3) (n=49)	-0.5 (10.0) (n=40)	53.2 (13.4) (n=45)	1.5 (5.8) (n=39)
LDL cholesterol	109.3 (33.2) (n=50)	2.6 (20.9) (n=44)	101.6 (31.1) (n=55)	0.5 (25.9) (n=49)	108.1 (35.6) (n=49)	-6.9 (15.8) (n=40)	108.2 (40.9) (n=45)	1.6 (19.2) (n=39)
Total cholesterol	187.6 (37.0) (n=79)	-1.7 (27.5) (n=71)	183.3 (41.8) (n=79)	7.8 (30.8) (n=70)	187.2 (41.0) (n=74)	-3.8 (20.0) (n=62)	188.3 (42.1) (n=80)	6.2 (26.6) (n=71)
Triglycerides	137.7 (116.1) (n=79)	-3.1 (93.4) (n=71)	136.3 (110.3) (n=79)	10.5 (101.9) (n=70)	109.4 (49.2) (n=74)	5.5 (34.1) (n=62)	122.3 (66.4) (n=80)	15.8 (64.3) (n=71)
Prolactin, ng/mL								
Females	7.3 (3.8) (n=48)	1.1 (4.4) (n=44)	8.9 (8.7) (n=50)	-0.3 (9.5) (n=46)	9.4 (6.4) (n=49)	4.6 (10.0) (n=47)	10.8 (7.2) (n=50)	6.1 (11.1) (n=48)
Males	7.3 (3.0) (n=34)	-0.6 (2.4) (n=32)	8.7 (4.4) (n=29)	-0.5 (2.8) (n=27)	7.0 (2.9) (n=26)	3.6 (6.7) (n=23)	7.6 (3.7) (n=30)	1.6 (3.5) (n=29)

Endpoint[a]	Placebo + placebo		Sertraline + placebo		Brexpiprazole + placebo		Brexpiprazole + sertraline	
	Baseline (Day 0)	Change to last visit	Baseline (Day 0)	Change to last visit	Baseline (Day 0)	Change to last visit	Baseline (Day 0)	Change to last visit
Prolactin >3x ULN, No. (%)[c]								
Females	–	0	–	0	–	0	–	0
Males	–	0	–	0	–	0	–	0
Orthostatic hypotension, No. (%)[d]	–	0	–	0	–	0	–	0
QTcF, ms	404.5 (19.7) (n=82)	-4.9 (16.9) (n=73)	406.2 (18.4) (n=79)	2.4 (18.1) (n=71)	401.2 (17.3) (n=75)	-1.6 (14.4) (n=66)	404.0 (19.7) (n=80)	1.5 (17.3) (n=73)
QTcF prolongation, No. (%)[e]	–	1/73 (1.4)	–	0	–	0	–	0
SAS total score	0.3 (0.6) (n=82)	-0.2 (0.6) (n=82)	0.3 (1.1) (n=78)	-0.2 (1.0) (n=78)	0.3 (0.9) (n=75)	-0.1 (1.0) (n=75)	0.3 (1.0) (n=80)	-0.1 (0.8) (n=80)
AIMS Movement rating score	0.1 (0.3) (n=82)	-0.1 (0.3) (n=82)	0.0 (0.2) (n=78)	0.0 (0.3) (n=78)	0.0 (0.2) (n=75)	0.0 (0.6) (n=75)	0.1 (0.7) (n=80)	-0.1 (0.7) (n=80)
BARS Global score	0.2 (0.5) (n=82)	-0.2 (0.5) (n=82)	0.2 (0.5) (n=78)	0.0 (0.7) (n=78)	0.2 (0.5) (n=75)	0.1 (0.8) (n=75)	0.3 (0.7) (n=80)	-0.1 (0.7) (n=80)

[a]Values are mean (SD) unless otherwise described as No. (%).

[b]Value at randomization (Week 1).

[c]At any post-baseline visit. ULN=13.13 ng/mL (males), 26.72 ng/mL (females).

[d]≥20 mmHg decrease in systolic blood pressure and ≥25 beats per minute increase in heart rate from supine to standing, at any post-baseline visit.

[e]New onset, >450 ms (men), >470 ms (women), at any post-baseline visit.

Abbreviations: AIMS=Abnormal Involuntary Movement Scale; BARS=Barnes Akathisia Rating Scale; BMI=body mass index; HDL=high-density lipoprotein; LDL=low-density lipoprotein; QTcF=QT interval as corrected by Fridericia's formula; SAS=Simpson–Angus Scale; ULN=upper limit of normal.