The Vasopressin V₁b Receptor Antagonist SSR149415 in the Treatment of Major Depressive and Generalized Anxiety Disorders: Results From 4 Randomized, Double-Blind, Placebo-Controlled Studies

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**ABSTRACT**

**Objective:** These studies were designed to evaluate the efficacy and tolerability of the first nonpeptide vasopressin V₁b receptor antagonist, SSR149415, in the treatment of major depressive disorder (MDD) and generalized anxiety disorder (GAD).

**Method:** Studies were randomized 8-week, double-blind, placebo-controlled trials evaluating 100- and 250-mg twice daily doses of SSR149415, placebo, and escitalopram 10 mg/day or paroxetine 20 mg/day, conducted from August 2006 through February 2008. Participants met the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision criteria for MDD or GAD. Baseline Montgomery-Asberg Depression Rating Scale (MADRS) and Hamilton Depression Rating Scale (HDRS) total scores were ≥24 and ≥18, respectively, and in the GAD trial baseline Hamilton Anxiety Rating Scale (HARS) score was ≥22. Primary efficacy variables included changes from baseline in total score on HDRS or HARS and MADRS, and the secondary variable included changes in the Clinical Global Impressions-Severity of Illness score (CGI-S).

A 4-week, double-blind, placebo-controlled study evaluating the effect of 100- and 250-mg twice daily doses of SSR149415 on the hypothalamic-pituitary-adrenal (HPA) axis in MDD patients was also conducted.

**Results:** In the GAD trial, SSR149415 did not separate from placebo on the primary (HARS—100 mg: P = 0.29; 250 mg: P = 0.21) and secondary (CGI-S—100 mg: P = 0.18; 250 mg: P = 0.24) outcome measures, while paroxetine demonstrated efficacy (HARS: P = .003; CGI-S: P = .01). In 2 MDD trials, SSR149415-treated patients did not show significant improvement from baseline on any outcome measure compared with placebo-treated patients (HDRS—100 mg: P = 0.21 and 0.48, respectively; 250 mg: P = 0.22 and 0.46, respectively; CGI-S—100 mg: P = 0.64 and 0.82, respectively; 250 mg: P = 0.33 and 0.08, respectively). In the third MDD study, SSR149415 250 mg (P = 0.04), but not escitalopram (P = 0.15), demonstrated significant improvement compared to placebo on the HDRS total score at week 8. SSR149415 had no deleterious effects on the HPA axis.

**Conclusions:** These studies demonstrate that SSR149415 may not be useful for the treatment of GAD and that its antidepressant potential needs to be further evaluated.

**Trial Registration:** ClinicalTrials.gov identifiers: NCT00374166 (Sanofi ID number: DFIS880), NCT00361491 (Sanofi ID number: DFIS5879), NCT00358631 (Sanofi ID number: DFIS5878), NCT01606384 (Sanofi ID number: PDYS467)

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Text Revision (DSM-IV-TR)\(^1\) criteria and confirmed by the semistructured Mini-International Neuropsychiatric Interview (MINI),\(^2\) or the semistructured MINI GAD Plus Module\(^3\) were enrolled into Sanofi protocols DFI5878 (ClinicalTrials.gov identifier: NCT00358631), DFI5879 (identifier: NCT00361491), DFI5880 (identifier: NCT00374166), and PDY5467 (identifier: NCT01606384). Eligible patients in all the trials were required to have a minimum Hamilton Depression Rating Scale (HDRS)\(^4\) or a Hamilton Anxiety Rating Scale (HARS)\(^5\) total score of 18 or 22 at screening and baseline visits, respectively. A minimum score of 4 (moderately ill) on the Clinical Global Impressions-Severity of Illness scale (CGI-S)\(^6\) at screening and baseline was also required. Additional details on the inclusion and exclusion criteria can be found on ClinicalTrials.gov.

**Study Designs**

Studies DFI5878 (in MDD patients) and DFI5880 (in GAD patients) were US, multicenter, randomized, double-blind, 4-parallel-group, placebo-controlled, Phase 2b studies with escitalopram or paroxetine as active control consisting of 3 segments (A, B, and C), conducted from July 2006 through December 2007 and from August 2006 through February 2008, respectively. Segment A was a 1-week, single-blind, placebo period. Segment B was an 8-week, double-blind period. Segment C was a 1-week drug-free follow-up period after study discontinuation or early termination (during Segment B). A total of 319 (DFI5878) or 328 (DFI5880) patients were randomized into Segment B via an interactive voice response system (IVRS) in a 1:1:1:1 ratio to 1 of the 4 treatment groups: placebo, SSR149415 (250 mg twice daily and 100 mg twice daily), and escitalopram (10 mg/day) (study DFI5878) or paroxetine (20 mg/kg/day) (study DFI5880) in a total of 24 or 36 active centers. The regions participating in this study were the Midwest, Northeast, South, and West.

Study DFI5879 (in MDD patients) was a multinational, multicenter, randomized, double-blind, 4-parallel-group, placebo-controlled, Phase 2b study with paroxetine as active control consisting of 3 segments (A, B, and C) conducted from August 2006 through September 2007. Segment A was a 1-week, single-blind, placebo period. Segment B was an 8-week double-blind period. Segment C was a 1-week drug-free follow-up period after study drug discontinuation or early termination (during Segment B). A total of 324 patients were randomized into Segment B via IVRS in a 1:1:1:1 ratio to 1 of the 4 treatment groups: placebo, SSR149415 (250 mg twice daily and 100 mg twice daily), and escitalopram (20 mg/day) (study DFI5879) or paroxetine (20 mg/kg/day) (study DFI5880) in a total of 24 or 36 active centers. The regions participating in this study were Argentina, Canada, Chile, Croatia, Bulgaria, Mexico, and Russia.

Study PDY5467 (in MDD patients) was a US randomized, double-blind, parallel-group, placebo-controlled study conducted from December 2006 through August 2008. The study consisted of 3 segments (A, B, and C). Segment A was a 1- to 4-week, drug-free, screening and baseline period. Segment B was a 4-week, double-blind period. After the last dose of double-blind study medication in Segment B, all patients had to enter Segment C, a 1-week, drug-free, follow-up period. A total of 100 patients were randomized into Segment B via IVRS in a 1:1:1 ratio to 1 of the 3 treatments groups: placebo and SSR149415 (250 mg twice daily and 100 mg twice daily) into a total of 3 US centers. A total of 73 randomized patients at 2 centers were retained for analysis, as serious Good Clinical Practice compliance issues were found at 1 center.

Patients were hospitalized the afternoon of day −4 and day 25. Standard 2-hour CRF tests were performed on days −2 and 27. Corticotropin-releasing factor (100-mg corticorelin ovine trifluate or Acthrel, Ferring Pharmaceuticals Inc, Suffern, New York) was administered at 4:00 pm on each day. An intravenous canula was placed at 3:00 pm, and blood samples for plasma cortisol and ACTH were collected at the following time points: (1) Prior to CRF administration at −60, −30, −15, and 0 minutes (or at 3:00, 3:30, 3:45 and 4:00 pm, just prior to administration of CRF); (2) After CRF administration at +5, +15, +30, +60, +90, and +120 minutes (or at 4:05, 4:15, 4:30, 5:00, 5:30 and 6:00 pm). Venous blood samples for ACTH and cortisol were collected into properly labeled tubes. Blood samples were kept on ice until centrifuged. Plasma was stored frozen at −20°C until assay. Adrenocorticotropic and cortisol concentrations were analyzed using highly sensitive radioimmunoassays.

Approval was obtained from regulatory authorities and national, regional, or investigational center ethics committees or institutional review boards, and written informed consent was obtained from each patient prior to the performance of study-specific procedures.

**Efficacy Evaluations**

For studies DFI5878 and DFI5879, the primary measure included changes from baseline to visit 7 (day 56) in the 17-item HDRS total score in the intent-to-treat (ITT) population. The main secondary efficacy variables were the change from baseline on the CGI-S item and the HDRS depressed mood item scores at visit 7 (day 56). The other main secondary criterion was the Montgomery-Asberg Depression Rating Scale (MADRS)\(^7\) total score.

For study DFI5880, the primary measure included changes from baseline to visit 7 (day 56) on the 14-item HARS total score in the ITT population. The main secondary efficacy variables were the change from baseline on the CGI-S. The other main secondary criterion was the MADRS total score.

For study PDY5467, the primary and main secondary pharmacodynamic endpoints were the basal, total, and
Statistical Analyses
For studies DFI5878, DFI5879, and DFI5880, the analyses of primary efficacy variable were performed on the ITT population as primary population. The primary efficacy variable, the change from baseline in the HARS or HDRS total score, was analyzed using a mixed-effect model repeated measure (MMRM)20 approach, under the missing-at-random framework. The treatment group factor in each of the studies had 4 levels (SSR149415 250 mg twice daily and placebo) and the factor visit had 5 levels (eg, visit 3 [day 7], visit 4 [day 14], visit 5 [day 28], visit 6 [day 42], and visit 7 [day 56]). This model, using all available postbaseline evaluations at day 56). This model, using all available postbaseline evaluations in Segment B, provided the baseline adjusted least-squares means (LS-means) estimates at day 56 by treatment group as well as the statistical significance of the primary efficacy comparison.

Pairwise comparisons between each dose of SSR149415 and placebo were made using the Bonferroni-Holm procedure.21 Student t tests were used to determine the statistical significance of the primary efficacy comparison. The analysis of covariance (ANCOVA) with missing data imputed using a last-observation-carried-forward (LOCF) method was performed and specified as a sensitive approach for the primary endpoint.

The main secondary efficacy variables were analyzed using MMRM as main approach (CGI-S) or ANCOVA at day 56 or last evaluation in Segment B, as no repeated measure was planned for this scale (MADRS). For study PDY5467, basal, total, and net integrated responses for cortisol at day 27 were analyzed using a 1-factor (treatment group) ANCOVA with respective corresponding response at day −2 as baseline covariate. The 95% confidence interval of the appropriate baseline adjusted LS-means difference versus placebo was provided for each dose. The secondary efficacy variables, the change from baseline to day 28 of quantitative variables with baseline interaction (HDRS total score and CGI-S), were analyzed using a MMRM approach.
Figure 1. Change From Baseline in HDRS (A and D), CGI-S (B and E), and MADRS (C and F) in a Randomized, Double-Blind, Placebo- and Escitalopram- or Paroxetine-Controlled Study of SSR149415

A. Study DFI5878

B. Study DFI5879

C.

D.

E.

F.

*Total score based on mixed-effect model repeated measure analysis, intent-to-treat population.

*Total score based on last-observation-carried-forward analysis of covariance, intent-to-treat population.

Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness scale, HDRS = Hamilton Depression Rating Scale, LS = least-squares, MADRS = Montgomery-Asberg Depression Rating Scale, SEM = standard error of the mean, SSR = SSR149415.
Patient Characteristics

Baseline demographic and clinical characteristics were relatively comparable among the studies and treatment groups (Table 1).

Efficacy

Study DFI5878. Patients in the SSR149415 250-mg but not in the 100-mg twice daily group had a significantly greater improvement in HDRS total score than patients in the placebo group (Figure 1A). The P value of .0244 from MMRM was below the .025 threshold given for Bonferroni-Hommel used as multiple comparison procedure. In contrast, the difference of −1.63 observed between the escitalopram group and the placebo group in the HDRS total score change from baseline at week 8 was not significant (P = .2088). Results obtained from LOCF ANCOVA were consistent with MMRM but not significant according to the Bonferroni-Hommel procedure for the comparison of SSR149415 250-mg twice daily group versus placebo (P = .0436). Analyses of the results for the main secondary efficacy variables showed that patients from the 2 SSR149415 groups and the escitalopram group displayed a similar improvement in CGI-S score that was numerically not larger than the one observed in patients from the placebo group (Figure 1B). The number of patients assessed with MADRS represented only 86% of the patients from the ITT population. Analysis of this secondary efficacy measure showed an improvement in each SSR149415 group as well as in the escitalopram group that was larger than the one observed in the placebo group, but only the effects of the latter group reached statistical significance (P = .0275; Figure 1C).

Study DFI5879. The differences between placebo and each SSR149415 dose on the primary variable with MMRM as well as with LOCF ANCOVA were not statistically significant (Figure 1D). The observed difference between placebo and each SSR149415 dose, 100 mg twice daily and 250 mg, on the HDRS total score change versus baseline represented, respectively, 25% and 27% of the effect observed between paroxetine and placebo. The assay sensitivity was established by a statistically significant effect between placebo and paroxetine (P = .0061). The observed difference between placebo and each SSR149415 dose on CGI-S score was not statistically significant (Figure 1E). The assay sensitivity was established by a statistically significant effect between placebo and paroxetine (P < .0001). Similarly, analysis of the MADRS score failed to reveal a statistically significant difference between placebo and any dose of SSR149415, while paroxetine produced a significant improvement on this secondary efficacy variable (P = .0007; Figure 1F).

Study DFI5880. The differences between placebo and each SSR149415 dose on the primary variable with MMRM, as well as with LOCF ANCOVA, were not statistically significant (Figure 2A). The observed difference between placebo and each SSR149415 dose, 100 mg twice daily and 250 mg, on the HDRS total score change versus baseline represented, respectively, 25% and 27% of the effect observed between paroxetine and placebo. The assay sensitivity was established by a statistically significant effect between placebo and paroxetine (P = .0013). The observed difference between placebo and each SSR149415 dose on CGI-S, HARS, and MADRS scores was not statistically significant (Figure 2B–F). The assay sensitivity was established by a statistically significant effect between placebo and paroxetine (P = .0139; Figure 2B).
and paroxetine ($P = .0034$). For the CGI-S score, the change from baseline to week 8 was not significantly different for any of the SSR149415 doses compared to placebo. In contrast, the change in CGI-S score was significantly greater in the paroxetine group ($P = .0139$; Figure 2B). For both HARS and CGI-S, statistically significant separation from placebo was observed from week 2 onward for the paroxetine group. Regarding the MADRS, there was no statistical difference between placebo and each SSR149415 dose on this secondary variable. This was in contrast to paroxetine, which improved significantly, albeit marginally, on the MADRS score at day 56 (Figure 2C).

**Study PDY5467.** Table 2 summarizes the results for basal, total, and net integrated cortisol response to CRF, respectively, at visit 13 (day 27) based on ANCOVA with visit 4 (day −2) corresponding response as covariate. Small dose-related increases in baseline-adjusted LS-means difference from placebo of basal and total cortisol responses to CRF were noted. For both basal and total cortisol responses, the differences versus placebo were significant in the SSR149415 250-mg twice daily group ($P = .0186$ and $P = .0331$, respectively) and marginally significant in the SSR149415 100-mg twice daily group ($P = .0858$ and $P = .0857$, respectively). Small decreases in baseline-adjusted LS-means difference from placebo of net cortisol response to CRF were noted. The differences versus placebo were not significant for either SSR149415 100-mg group ($P = .6815$ and $P = .4936$ for 100-mg and 250-mg twice daily, respectively). Analysis of the results for basal, total, and net integrated ACTH response shows small, albeit nonsignificant, increases in baseline-adjusted LS-means of basal, total, and net ACTH responses to CRF (data not shown). Finally, results for the HDRS total score based on the MMRM analysis revealed that patients in both SSR149415 groups had greater mean improvements from baseline in HDRS total score and CGI-S than patients in the placebo group, although the differences were not significant (HDRS: $P = .3408$ and $P = .2653$; CGI-S: $P = .6420$ and $P = .33$ for 100 mg and 250 mg twice daily, respectively).

**Safety**

Table 3 summarizes all adverse events (AEs) occurring in patients in any study and treatment group. There was no statistically significant difference between placebo and SSR149415. The most frequent AEs observed in all groups were headache, nausea, and dizziness. Few events were considered severe (highest proportion was 2.5% observed in study DFI5879 at SSR149415 250-mg twice daily). Withdrawal rates due to AEs ranged from 3.6% to 13.6%, with the highest rate observed for SSR149415 250-mg twice daily in study DFI5879 and paroxetine 20-mg/day in study DFI5880. No deaths occurred during either study. Increase in liver function tests was the main safety observation, with 5 patients in the 100-mg twice daily group and 5 patients in the 250-mg twice daily group showing a combined increase of transaminase and bilirubin. However, none of these patients had an associated total bilirubin ≥ 2, which is in the upper limit of normal range. In studies DFI5879 and DFI5880, 10 patients in the SSR149415 groups had a least 1 postbaseline PR interval that ranged from 220 to 255 ms. No patients in the SSR149415 treatment groups had QTcF intervals ≥ 500 ms. One patient (250 mg twice daily) had an increase in QTcF interval > 60 ms (66 ms), although the absolute QTcF interval was not prolonged (425 ms).

**DISCUSSION**

This is the first report on the effects of a vasopressin V$_{1b}$ receptor antagonist in the treatment of MDD and GAD in 3 double-blind, placebo-controlled trials. Results showed that SSR149415 failed to demonstrate efficacy in the treatment of these conditions.

Of the 3 studies, study DFI5878 demonstrated a significant antidepressant effect for the higher SSR149415 dose (250 mg twice daily) on the primary endpoint (HDRS) as early as week 1 of treatment but not on MADRS at week 8. Moreover, this study failed to show significant differences for the active comparator (escitalopram) versus placebo at any time point in the ITT population. Studies DFI5879 and DFI5880 determined that SSR149415 100-mg and 250-mg twice daily were not superior in efficacy to placebo for the treatment of MDD and GAD, respectively. The active comparator arm, paroxetine, in both of these studies showed statistical separation from placebo and demonstrated that robust signal detection was obtained. Whether the lack of efficacy of SSR149415 is specific to this particular compound, due to the dose employed, or is indicative of a more specific receptor interaction.

| Table 2. Summary of Cortisol Responses to CRF Administration Following Treatment With SSR149415 or Placebo in Major Depressive Disorder Patients (PDY5467)$^a$ |
|-----------------|-----------------|-----------------|-----------------|
| **Response**    | **Placebo**     | **SSR149415 100 mg Twice Daily** | **SSR149415 250 mg Twice Daily** |
| Basal integrated cortisol, nmol/L | | | |
| LS-Mean (SE) change from day −2 at day 27 | −2,025.37 (895.53) | −11.53 (714.61) | 874.93 (787.77) |
| $P$ value vs placebo | .0858 | .0186 | |
| Total integrated cortisol, nmol/L | | | |
| LS-Mean (SE) change from day −2 at day 27 | −2,180.70 (1,877.11) | 2,078.31 (1,466.84) | 3,264.52 (1,602.82) |
| $P$ value vs placebo | .0857 | .0331 | |
| Net integrated cortisol, nmol/L | | | |
| LS-Mean (SE) change from day −2 at day 27 | 2,837.12 (2,207.03) | 1,670.27 (1,746.62) | 807.10 (1,930.32) |
| $P$ value vs placebo | .6815 | .4936 | |

$^a$ $P$ values are based on covariance analysis adjusted for day −2 response. Abbreviations: CRF = corticotropin-releasing factor, LS = least-squares, SE = standard error.
Table 3. Effect of Treatment With SSR149415, Escitalopram, Paroxetine, or Placebo on the Incidence of Adverse Events

<table>
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<th>Adverse Event, n (%)</th>
<th>Study DF15878 Placebo</th>
<th>Study DF15878 SSR 100 mg</th>
<th>Study DF15878 SSR 250 mg</th>
<th>Study DF15878 Escitalopram 10 mg</th>
<th>Study DF15878 Paroxetine 10 mg</th>
<th>Study DF15879 Placebo</th>
<th>Study DF15879 SSR 100 mg</th>
<th>Study DF15879 SSR 250 mg</th>
<th>Study DF15879 Escitalopram 10 mg</th>
<th>Study DF15879 Paroxetine 10 mg</th>
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<td>12 (14.6)</td>
<td>5 (6.2)</td>
<td>13 (16.3)</td>
<td>8 (9.9)</td>
<td>3 (3.8)</td>
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<td>9 (11.0)</td>
<td>4 (16.7)</td>
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<td>3 (3.7)</td>
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<td>15 (19.5)</td>
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<td>3 (3.7)</td>
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*SSR doses were administered twice daily.

Abbreviations: NA = not assessed, SSR = SSR149415.
general failure of this particular class of drugs in depression and anxiety disorders remains unknown. There have been several other V1b receptor antagonists studied by other pharmaceutical companies to date; however, none of them have made it yet to advanced clinical development for stress-related disorders.22

The absence of beneficial effects of SSR149415 over placebo in anxiety and depression symptoms is somewhat surprising, given the central role that the vasopressin system, in particular via the V1b receptor, is hypothesized to play in the neuroendocrine response to stress, notably through the modulation of the HPA axis.23,24 Available information regarding the pharmacokinetic properties of SSR149415 and preclinical studies suggest that appropriate blood levels were obtained in this clinical trial. However, it is important to note that SSR149415 was tested in the efficacy studies at doses (ie, 100 mg and 250 mg twice daily) that had only a marginal effect on net cortisol response to a CRF challenge, a putative marker of drug activity, as shown in study PDY5467, although the drug reduced basal cortisol levels significantly at 250 mg. Doses higher than 250 mg/day or twice daily of SSR149415 have been shown to significantly attenuate this response in a Phase I study.25 The absence of clear inhibition of cortisol levels at the current doses might suggest insufficient vasopressin blockade to achieve therapeutically effective human V1b receptors available. This study has several limitations, which may account to a certain degree for the lack of efficacy of SSR149415 in the current trials, notably in the GAD trial. V1b receptors may be particularly activated during acute stress and early phases of anxiety disorders,5 and blocking these receptors may have limited efficacy in chronic states in which stable anxiety levels have been established. This idea is substantiated by studies in animals showing that SSR149415 elicited robust anxiolytic-like activity in models relating to certain aspects of acute or posttraumatic stress, while it produced limited efficacy in procedures claimed to model aspects of GAD.12 Therefore, the V1b receptor may play an important role in the early stages of illness, and antagonists may be best utilized during this period or in stress-induced psychiatric disorders, such as acute or posttraumatic stress disorder. Moreover, it is possible that blocking only 1 system, such as vasopressin, may not be sufficient to achieve a therapeutic response with regard to anxiety and depression. Common to the current trials is that a very specific mechanism is probed in patient groups that are certainly heterogeneous on observation levels ranging from psychopathology to biomarkers and DNA-sequence variations. Thus, future trials exploring the potential of V1b receptor antagonists to use biomarkers and gene tests to make sure that the study samples are enriched with patients in whom excessive vasopressin V1b signaling is one of the major pathogenetic factors.22 Clearly, it is still too early to draw definitive conclusions on the therapeutic potential of V1b antagonists in anxiety and depressive disorders. They deserve further studies as either adjunctive therapy or monotherapy.

**Drug names:** escitalopram (Lexapro and others), fluoxetine (Prozac and others), paroxetine (Paxil, Pexeva, and others).

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**Study investigators:** See Supplementary eAppendix 1 at PSYCHIATRIST.COM for a complete list of study investigators.

**Potential conflicts of interests:** Ms Beeské and Dr Griebel are employees of Sanofi. Dr Stahl has served as a consultant for Acadia, AstraZeneca, Avanir, BioMarin, Bristol-Myers Squibb, Cenerex, Dey, Eli Lilly, Forest, GenOmind, GlaxoSmithKline, Johnson & Johnson, Jazz, Lundbeck, Merck, Neurionetics, Novartis, Noven, Ono, Orexigen, Otsuka, PamLab, Pfizer, PgdHealth, RCT Logic, Rexahn, Roche, Servier, Shire, Solvay, Sunovion, Titus and Valeant; has served on speakers bureaus for Arbor Scientia, AstraZeneca, Eli Lilly, Forest, Johnson & Johnson, Merck, Neuroscience Education Institute, Pfizer, Servier and Sunovion; and has received research and/or grant support from AstraZeneca, Cenerex, Eli Lilly, Forest, GenOmind, Merck, Neurionetics, PamLab, Pfizer, Roche, Schering-Plough, Seppracor, Servier, Shire, Sunovion, Torrent, and Trovis.

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**Previous presentations:** Findings of the studies were presented in part at the 19th Neuropharmacology Conference on Neuropeptides; October 14–16, 2009; Chicago, Illinois; and the Annual Meeting of the American College of Neuropsychopharmacology; December 4–8, 2011; Waikoloa, Hawaii.

**Additional information:** The Sanofi database is not publicly accessible. Readers may request access to the data by contacting Dr Griebel.

**Supplementary material:** eAppendix 1 is available at PSYCHIATRIST.COM.

**REFERENCES**


The V₁b Receptor Antagonist SSR149415 for MDD and GAD


See supplementary material for this article at PSYCHIATRIST.COM.
Supplementary Material

Article Title: The Vasopressin V1b Receptor Antagonist SSR149415 in the Treatment of Major Depressive and Generalized Anxiety Disorders: Results From 4 Randomized Double-Blind, Placebo-Controlled Studies

Author(s): Guy Griebel, PhD; Sandra Beeské, MS; and Stephen M. Stahl, MD

DOI Number: 10.4088/JCP.12m07804

List of Supplementary Material for the article

1. eAppendix 1 Complete list of study investigators

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This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.
Supplementary eAppendix 1

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