**APPENDIX 1**

**List of adverse events related to sexual dysfunction based on MedDRA v14.1 preferred term**

Anorgasmia

Disturbance in sexual arousal

Dyspareunia

Ejaculation delayed

Ejaculation disorder

Ejaculation failure

Erectile dysfunction

Female orgasmic disorder

Female sexual arousal disorder

Female sexual dysfunction

Inadequate lubrication

Libido decreased

Libido disorder

Loss of libido

Male orgasmic disorder

Male sexual dysfunction

Organic erectile dysfunction

Orgasm abnormal

Orgasmic sensation decreased

Premature ejaculation

Psychogenic erectile dysfunction

Sexual aversion disorder

Sexual dysfunction

Sexual inhibition

Vaginismus

Vulvovaginal dryness

**APPENDIX 2**

**Short-term (6–8 weeks in duration) clinical trials of vortioxetine in patients with major depressive disorder or generalized anxiety disorder**

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| **Completed Phase 2 and 3 Major Depressive Disorder Studies** |
| **Study No./** **Region**  | **Study Design/****Duration** | **Diagnosis and Main Inclusion Criteria** | **Study Drug Doses (mg)** (a) | **No. of Subjects Treated** |
| NCT00839423Europe, Australia, Canada, Asia  | Randomized, double-blind, parallel-group, placebo-controlled, active-referenced (venlafaxine), fixed-dose / 6 weeks + 2 weeks taper-down/ discontinuation period  | MDD, 18–65 years, MADRS ≥30, men and women  | Vortioxetine: 5 or 10Venlafaxine: 225placebo | Vortioxetine 5 mg: 108Vortioxetine 10 mg: 100Venlafaxine 225 mg: 113Placebo: 105 |
| NCT00635219Europe, Canada, Asia, Australia,  | Randomized, double-blind, parallel-group, placebo-controlled, active-referenced (duloxetine), fixed-dose / 8 weeks + 1 week taper-down (only duloxetine)  | MDD, 18–75 years, MADRS ≥26, men and women  | Vortioxetine: 2.5, 5 or 10Duloxetine: 60Placebo | Vortioxetine 2.5 mg: 155Vortioxetine 5 mg: 157Vortioxetine 10 mg: 151Duloxetine 60 mg: 155Placebo: 148 |
| NCT00735709Europe, Asia, Australia, South Africa  | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 8 weeks | MDD, 18–75 years, MADRS ≥26, men and women  | Vortioxetine: 1, 5, or 10Placebo | Vortioxetine 1 mg: 140Vortioxetine 5 mg: 140Vortioxetine 10 mg: 139Placebo: 140 |
| NCT01140906Europe, South Africa  | Randomized, double-blind, placebo-controlled, active-referenced (duloxetine), parallel-group, fixed-dose / 8 weeks + 2 weeks discontinuation period  | MDD, 18–75 years, MADRS ≥26 and CGI-S ≥4, men and women  | Vortioxetine: 15 or 20Duloxetine: 60Placebo | Vortioxetine 15 mg: 152Vortioxetine 20 mg: 151Duloxetine 60 mg: 147Placebo: 157 |
| NCT01153009United States  | Randomized, double-blind, placebo-controlled, active-referenced (duloxetine), parallel-group, fixed-dose / 8 weeks + 2 weeks discontinuation period  | MDD, 18–75 years, MADRS ≥26 and CGI-S ≥4, men and women  | Vortioxetine: 15 or 20Duloxetine: 60Placebo | Vortioxetine 15 mg: 147Vortioxetine 20 mg: 154Duloxetine 60 mg : 152Placebo: 161 |
| NCT01163266United States | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 8 weeks + 2 weeks discontinuation period  | MDD, 18–75 years, MADRS ≥26 and CGI-S ≥4, men and women  | Vortioxetine: 10 or 20Placebo | Vortioxetine 10 mg: 154Vortioxetine 20 mg: 148Placebo: 155 |
| NCT01179516United States | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 8 weeks | MDD, 18–75 years, MADRS ≥26 and CGI-S ≥4, men and women  | Vortioxetine: 10 or 15Placebo | Vortioxetine 10 mg: 143Vortioxetine 15 mg: 142Placebo: 149 |
| NCT00672958United States | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 6 weeks + 2 weeks discontinuation period  | MDD, 18–75 years, MADRS ≥30, men and women  | Vortioxetine: 5Placebo | Vortioxetine 5 mg: 299Placebo: 298 |
| NCT00672620United States | Randomized, double-blind, placebo-controlled, parallel-group, active-referenced (duloxetine), fixed-dose / 8 weeks + 1 week taper-down (only duloxetine)  | MDD, 18–75 years, MADRS ≥22, men and women  | Vortioxetine: 2.5 or 5Duloxetine: 60Placebo | Vortioxetine 2.5 mg: 153Vortioxetine 5 mg: 153Duloxetine 60 mg: 152Placebo: 153 |
| NCT00811252Europe, Canada, United States | Randomized, double-blind, parallel-group, placebo-controlled, active-referenced (duloxetine), fixed dose, in elderly subjects / 8 weeks + 1 week taper-down (only duloxetine) | MDD, ≥65 years, MADRS ≥26, men and women | Vortioxetine: 5Duloxetine: 60Placebo | Vortioxetine 5 mg: 156Duloxetine 60 mg: 151 |
| **Completed Phase 3 Generalized Anxiety Disorder Studies** |
| NCT00730691United States | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose, active-reference (duloxetine) / 8 weeks + 2 weeks taper-down discontinuation period | GAD, 18–65 years, HAM-A ≥20, HAM-A ≥2 on item 1 (anxious mood) and item 2 (tension), men and women | Vortioxetine: 2.5, 5, or 10Duloxetine: 60Placebo | Vortioxetine 2.5 mg: 156Vortioxetine 5 mg: 155Vortioxetine 10 mg: 156Duloxetine 60 mg: 154Placebo: 155 |
| NCT00731120United States | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 8 weeks | GAD, ≥18 years, HAM-A ≥20, HAM-A ≥2 on item 1 (anxious mood) and item 2 (tension), men and women | Vortioxetine: 2.5 or 10Placebo | Vortioxetine 2.5 mg: 151Vortioxetine 10 mg: 152Placebo: 153 |
| NCT00734071United States | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 8 weeks | GAD, ≥18 years, HAM-A ≥20, HAM-A ≥2 on item 1 (anxious mood) and item 2 (tension), men and women | Vortioxetine: 5Placebo | Vortioxetine 5 mg: 148Placebo: 151 |
| NCT00744627Europe | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 8 weeks | GAD, ≥18 years, HAM-A ≥20, HAM-A ≥2 on item 1 (anxious mood) and item 2 (tension), men and women | Vortioxetine: 5Placebo | Vortioxetine 5 mg: 150Placebo: 150 |
| CGI-S=Clinical Global Impression-Severity of Illness, GAD=generalized anxiety disorder, HAM-A=Hamilton Anxiety Scale, MADRS=Montgomery-Åsberg Depression Rating Scale, MDD=major depressive disorder.(a) Route of administration was oral. |