# Synopsis – Study 10200

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| **Title of Study**<br>A 6-month double-blind, risperidone-referenced, flexible-dose, parallel-group extension study of bifeprunox in patients with schizophrenia |
| **Investigators**<br>22 investigators in 8 countries<br>*Signatory investigator* – Jozef Peuskens, Professor, MD, PhD, University Clinic Sint Jozef, Kortenberg, Belgium |
| **Study Centres**<br>22 centres – 3 in Belgium, 2 in Finland, 2 in Greece, 1 in Hong Kong, 1 in Malaysia, 4 in the Philippines, 5 in Spain, and 4 in Thailand |
| **Publications**<br>None (as of the date of this report) |
| **Study Period**<br>*First patient first visit* – 8 September 2004<br>*Last patient last visit* – 21 March 2006 |
| **Objectives**<br>• *Primary objective:*<br>– to investigate the long-term safety and tolerability of flexible doses of bifeprunox, compared to flexible doses of risperidone, over a 6-month treatment period, in patients with schizophrenia having completed lead-in Study 10199<br>• *Secondary objective*:<br>– to investigate the long-term efficacy of flexible doses of bifeprunox, compared to flexible doses of risperidone, over a 6-month treatment period, in patients with schizophrenia having completed lead-in Study 10199 |
| **Methodology**<br>• Multinational, multi-centre, randomised, double-blind, parallel-group, active-comparator (risperidone), flexible-dose, 6-month extension study in patients with schizophrenia who had completed 6 months of double-blind treatment with flexible doses of bifeprunox (30 or 40 mg/day) or risperidone (4 or 6 mg/day) in lead-in Study 10199.<br>• Patients who had received bifeprunox in lead-in Study 10199 continued to receive bifeprunox, and patients who had received risperidone in lead-in Study 10199 continued to receive risperidone in extension Study 10200.<br>• The dose was flexible (30 or 40 mg/day bifeprunox and 4 or 6 mg/day risperidone) on the basis of the response and tolerability, as judged by the investigator.<br>• Efficacy and safety data were collected throughout the study at monthly intervals.<br>• A safety follow-up visit was scheduled for 1 week after completion of the study or after withdrawal from the study. |

**Number of Patients Planned and Analysed**

- 160 patients were anticipated to be enrolled in extension Study 10200: 80 in each treatment group.
- 108 patients completed lead-in Study 10199 and were eligible for enrolment.
- Patient disposition in extension Study 10200 is tabulated below:

| | BX | | RIS | | Total | |
|---|---|---|---|---|---|---|
| | n | (%) | n | (%) | n | (%) |
| Patients randomised[a] | 35 | | 58 | | 93 | |
| **Patients treated (all-patients-treated set (APTS)):** | 35 | | 58 | | 93 | |
| Patients completed | 22 | (62.9) | 43 | (74.1) | 65 | (69.9) |
| Patients withdrawn | 13 | (37.1) | 15 | (25.9) | 28 | (30.1) |
| **Primary reason for withdrawal:** | | | | | | |
| Adverse event(s) | 3 | (8.6) | 6 | (10.3) | 9 | (9.7) |
| Lack of efficacy | 3 | (8.6) | 3 | (5.2) | 6 | (6.5) |
| **Analysis sets:** | | | | | | |
| All-patients-treated set (APTS)[b] | 35 | | 58 | | 93 | |
| Extended all-patients-treated set (APTSX)[b] | 161 | | 171 | | 332 | |
| Full-analysis set (FAS)[b] | 35 | | 58 | | 93 | |

n = number of patients; % = percentage of patients within treatment group

a Patients were randomised at entry into lead-in Study 10199 and continued on the same treatment and dose in extension Study 10200 without re-randomisation

b For definitions of the analysis sets, see *Statistical Methods*

**Diagnosis and Main Inclusion Criteria**

In- and outpatients, aged 18 to 75 years (extremes included) at inclusion into lead-in Study 10199, with a primary diagnosis of schizophrenia according to DSM-IV-TR criteria, who had completed 6 months of double-blind treatment with 30 or 40 mg/day bifeprunox or 4 or 6 mg/day risperidone in lead-in Study 10199.

At inclusion into lead-in Study 10199, the patients had schizophrenia in an acute phase, that is, they had a PANSS total score between 70 and 120 (extremes included) and a score ≥4 on at least two of the following four PANSS items: P2 (*conceptual disorganisation*), P3 (*hallucinatory behaviour*), P6 (*suspiciousness*), G9 (*unusual thought content*). Patients also had a CGI-S score ≥4 (*moderately ill*).

**Investigational Product, Dose and Mode of Administration, Batch Number**

Bifeprunox – flexible doses of 30 or 40 mg once daily; capsules, orally; capsule batch Nos. E02499-163E, -297E, -412E (10 mg); E02499-166E, -298E, -413E, -414E (20 mg)

**Duration of Treatment**

6 months of double-blind treatment after 6 months of double-blind treatment in lead-in Study 10199

**Reference Therapy, Dose and Mode of Administration, Batch Number**

*Risperidone* – flexible doses of 4 or 6 mg once daily; capsules, orally; capsule batch Nos. E02499-169E, -311E, -415E (2 mg), E02499-171E, -312E, -416E (4 mg)

**Criteria for Evaluation – Efficacy**

Positive and Negative Syndrome Scale (PANSS) total score, PANSS Positive Symptom subscale score, PANSS Negative Symptom subscale score, PANSS General Psychopathology subscale score, Brief Psychiatric Rating Scale (BPRS) total score, BPRS psychosis cluster score, Clinical Global Impression – Severity of Illness (CGI-S) and – Global Improvement (CGI-I) scores, and Calgary Depression Scale for Schizophrenia (CDSS) score

**Criteria for Evaluation – Safety**

Adverse events, extrapyramidal symptoms (Simpson-Angus Scale (SAS), Barnes Akathisia Scale (BAS)), and Abnormal Involuntary Movements Scale (AIMS)), clinical safety laboratory tests, vital signs, weight, body mass index (BMI), electrocardiograms (ECGs), and physical and neurological examinations

**Statistical Methods**

- The following analysis sets were used:
  - *all-patients-treated set* (APTS) – all randomised patients who completed lead-in Study 10199 and took at least one dose of double-blind investigational medicinal product (IMP) in extension Study 10200
  - *extended all-patients-treated set* (APTSX) – all randomised patients in lead-in Study 10199 who took at least one dose of double-blind IMP in lead-in Study 10199
  - *full-analysis set* (FAS) – all patients in the APTS who had at least one valid assessment of PANSS total score in extension Study 10200; that is, one assessment after the Termination Visit in lead-in Study 10199
- Baseline was defined as the baseline in lead-in Study 10199, unless otherwise stated.
- Efficacy analyses were conducted using the FAS. Only data from extension Study 10200 are described and discussed, although data from lead-in Study 10199, for patients who continued in Study 10200, are included for completeness of the graphical presentations.
- Safety analyses were conducted using the APTSX when the entire period of exposure (Months 1 to 12) was considered and using the APTS when only the extension period (Months 7 to 12) was considered.
- For all efficacy scales, changes from baseline (entry into lead-in Study 10199) during the 6-month treatment period in extension Study 10200 were analysed by visit using an analysis of covariance (ANCOVA) model with treatment and centre as factors and the baseline score as a covariate. Estimated treatment differences are presented with 95% confidence intervals. The analysis of the CGI-I score (which has no baseline value) used the CGI-S baseline score as a covariate in the ANCOVA model along with terms for treatment and centre.
- Responder rates based on the PANSS total score (≥25%, ≥35%, ≥45%, or ≥55% reduction from baseline (entry into lead-in Study 10199)) and the CGI-I score (score ≤2) are presented as histograms and were analysed using Fisher's exact test.
- The incidences of all adverse events, adverse events leading to withdrawal, and serious adverse events (SAEs) were tabulated by primary system organ class (SOC) and preferred term. In addition, adverse events were tabulated by preferred term and intensity categories as were all adverse events that were considered related to IMP by the investigators.
- The incidences (proportion of patients with new events) and prevalences (proportion of patients with new or ongoing events) of the adverse events with an incidence or prevalence ≥5% in any 3-month interval were tabulated for 3-month intervals.
- Newly-emergent adverse events, a subset of adverse events disregarding adverse events that were present at any time point (including baseline (entry into lead-in Study 10199)) during the lead-in study, were tabulated.
- Changes from baseline (entry into lead-in Study 10199) to each assessment in extrapyramidal symptoms (EPS), based on the SAS, BAS, and AIMS scores, were summarised for the APTSX using descriptive techniques. An ANCOVA model, with treatment and centre as fixed factors and the baseline total score as a covariate, was used to test for treatment group differences both for the scores at endpoint and for the maximal scores during double-blind treatment.
- Absolute values and changes from baseline (entry into lead-in Study 10199) to each assessment in clinical safety laboratory tests, vital signs, weight, and ECG parameters were summarised using descriptive techniques. Values that were potentially clinically significant (PCS) were flagged and tabulated, as were clinical safety laboratory values that were outside reference range. Weight, BMI, high density lipoprotein (HDL) cholesterol, and triglycerides changes from baseline (entry into lead-in Study 10199) were analysed by visit using an ANCOVA model with terms for baseline value, treatment, and centre as the factors, and presented with 95% confidence intervals for the estimated treatment differences.

**Demography of Study Population**

- The ratio of men to women was 2 to 1, and the mean age was 39 years (ranging from 19 to 63 years); 62% of the patients were Asian and 38% of the patients were Caucasian.
- The patients in the APTS were similar to those in the APTSX in terms of sex, age, schizophrenia history (diagnosis, duration, and number of prior episodes), concurrent illnesses, and physical and neurological examinations, overall and between treatment groups. Small differences were noted in terms of race and mean weight; the differences were not considered to be clinically relevant.

**Efficacy Results**

The mean baseline PANSS total score, mean PANSS total score at entry into extension Study 10200, and the mean change from baseline (entry into lead-in Study 10199) to Month 12 are summarised below:

| | n | BX | n | RIS |
|---|---|---|---|---|
| **PANSS total score (FAS, OC)** | | | | |
| Mean at baseline in lead-in Study 10199 (standard deviation (SD)) | 35 | 92 (13) | 58 | 92 (13) |
| Mean at entry into extension Study 10200 (SD) | 35 | 62 (19) | 58 | 55 (17) |
| Mean change from baseline (entry into lead-in Study 10199) to Month 12 (SD) | 22 | -36 (21) | 43 | -42 (20) |

- The mean PANSS total score decreased from baseline (entry into lead-in Study 10199) in both treatment groups throughout the 12-month treatment period (Studies 10199 and 10200) (FAS, OC). The mean changes from baseline in PANSS total score to Week 6, Month 3, and Month 12 were -26, -30, and -36, respectively, in the bifeprunox group, and -31, -33, and -42, respectively, in the risperidone group (FAS, OC). The differences between the treatment groups were statistically significantly in favour of risperidone at Months 8, 10, and 11 for the OC, at Months 9, 10, and 12 for the LOCF, and at Months 8 to 12 for the POCF (FAS, ANCOVA).
- The mean PANSS Positive Symptoms subscale score, PANSS Negative Symptoms subscale score, PANSS General Psychopathology subscale score, BPRS total score, and BPRS Psychosis Cluster score generally followed the same pattern as that of the PANSS total score. The differences between the treatment groups were numerically in favour of risperidone at all time points and statistically significantly so at some time points (FAS, OC, ANCOVA).
- The mean CDSS total scores were low in both treatment groups throughout the 6-month extension study (FAS, OC).
- The mean CGI-S score remained stable in the bifeprunox group and decreased slightly in the risperidone group during the 6-month treatment period in extension Study 10200 (FAS, OC). The differences between the treatment groups were statistically significantly in favour of risperidone at Months 8 and 11 (FAS, OC, ANCOVA).
- The mean CGI-I score increased slightly in the bifeprunox group during the 6-month treatment period in extension Study 10200 (FAS, OC). The mean CGI-I score increased from entry into extension Study 10200 (Month 6) to Month 7 in the risperidone group after which it decreased slightly during the remainder of the 6-month treatment period in extension Study 10200 (FAS, OC). The differences between the treatment groups were statistically significantly in favour of risperidone at Months 8, 10, and 11 (FAS, OC, ANCOVA).
- The proportions of patients categorised as responders (patients with a ≥25%, ≥35%, ≥45%, or ≥55% reduction from baseline (entry into lead-in Study 10199) in PANSS total score or with a CGI-I score ≤2) were numerically larger in the risperidone group than in the bifeprunox group at all time points during the 6-month treatment period in extension Study 10200. The differences between the treatment groups were statistically significantly different at some time points (FAS, OC, ANCOVA).

**Safety Results**

- The adverse event incidence is summarised below:

| | 10199 + 10200 (APTSX) | | | | 10200 (APTS) | | | |
|---|---|---|---|---|---|---|---|---|
| | BX | | RIS | | BX | | RIS | |
| | n | (%) | n | (%) | n | (%) | n | (%) |
| Patients who died | | | 3 | | | | | |
| Patients with serious AEs (SAEs) | 47 | 29 | 35 | 20 | 7 | 20 | 10 | 17 |
| Patients with AEs leading to withdrawal | 51 | 32 | 50 | 29 | 3 | 9 | 6 | 10 |
| Patients with AEs | 139 | 86 | 151 | 88 | 24 | 69 | 43 | 74 |
| Total number of SAEs | 61 | | 47 | | 10 | | 14 | |
| Total number of AEs | 680 | | 818 | | 67 | | 136 | |

n = number of patients; % = percentage of patients within treatment group

- For the APTSX, the total accrued exposure from entry into lead-in Study 10199 was 49 patient-years in the bifeprunox group and 75 patient-years in the risperidone group. The *mean* number of days exposed to IMP was lower in the bifeprunox group (116 days) than in the risperidone group (166 days), as was the *median* number of days (62 and 130 days, respectively). At each scheduled visit during the 12-month study period, ≥70% of the patients in the bifeprunox group received the high dose (40 mg/day) at each visit and ≥50% of the patients in the risperidone group received the high dose (6 mg/day) at each visit.
- For the APTS, the total accrued exposure since entry into extension Study 10200 was 15 patient-years in the bifeprunox group and 24 patient-years in the risperidone group. The *mean* number of days exposed to IMP during the extension study in the bifeprunox group (155 days) was similar to that in the risperidone group (153 days), as was the *median* number of days exposed (175 and 178 days, respectively).
- No patients died during the 6-month treatment period in extension Study 10200. Three patients (all in the risperidone group) died during lead-in Study 10199. The patients died from diabetes mellitus, a fall from a building, and suicide.
- In all patients during the 12-month treatment period in Studies 10199 and 10200 (APTSX), there were no major differences between treatment groups in the overall incidences of adverse events or in the proportions of patients who withdrew due to adverse events. One or more adverse events were reported by 87% of the patients and 30% withdrew due to adverse events.
- During the 6-month treatment period in extension Study 10200 (APTS), there were no major differences between treatment groups in the overall incidences of adverse events or in the proportions of patients who withdrew due to adverse events. One or more adverse events were reported by 69% and 74% of the patients in the bifeprunox and risperidone groups, respectively, and 10% in each treatment group withdrew due to adverse events.
- In the bifeprunox group, the SOC with the highest incidence of adverse events was *psychiatric disorders*. During the 12-month treatment period, the incidence was similar to the incidence in the risperidone group but during the 6-month treatment period in extension Study 10200, the incidence was slightly higher in the bifeprunox group. The incidence of *gastrointestinal disorders* was higher in the bifeprunox group than in the risperidone group during the 12-month treatment period; this difference was not seen during the 6-month treatment period in extension Study 10200. Both during the 12-month treatment period and during the 6-month treatment period in extension Study 10200, the incidences of *nervous system disorders* and *infections and infestations* were higher in the risperidone group than in the bifeprunox group while the incidence of *investigations* was higher in the bifeprunox group than in the risperidone group.
- In the bifeprunox group during the 12-month treatment period (APTSX), the adverse events with the highest incidences (≥15%) were insomnia, vomiting, nausea, agitation, and weight decreased.
- In the risperidone group during the 12-month treatment period (APTSX), the adverse events with the highest incidences (≥15%) were insomnia, weight increased, extrapyramidal disorder, and akathisia.

**Safety Results – Continued**

- The incidences of the adverse events with an incidence of ≥15% in either treatment group during the 12-month treatment period were (bifeprunox *versus* risperidone):
  - insomnia (29% *vs* 32%)
  - vomiting (23% *versus* 10%)
  - nausea (22% *versus* 9%)
  - agitation (17% *versus* 13%)
  - weight decreased (17% *versus* 4%)
  - weight increased (8% *versus* 23%)
  - extrapyramidal disorder (7% *versus* 19%)
  - akathisia (4% *versus* 18%)
- During the 6-month treatment period in extension Study 10200 (APTS), the adverse events with the highest incidences (≥10%) in the bifeprunox group were insomnia, agitation, weight increased, and psychotic disorder.
- During the 6-month treatment period in extension Study 10200 (APTS), the adverse events with the highest incidences (≥10%) in the risperidone group were insomnia, agitation, and weight increased.
- The incidences of the adverse events with an incidence of ≥10% in either treatment group during the 6-month treatment period in extension Study 10200 were (bifeprunox *versus* risperidone):
  - insomnia (23% *versus* 21%)
  - agitation (17% *versus* 12%)
  - weight increased (17% *versus* 10%)
  - psychotic disorder (11% *versus* 7%)
- In an analysis of the incidence and prevalence of adverse events in 3-month intervals from baseline (entry into Study 10199), the most clear trends in the bifeprunox group were seen for nausea, vomiting, constipation, and headache for which the incidences as well as the prevalences decreased considerably; that is, most of these events occurred during the first 3-month interval and had a duration shorter than 3 months. The incidences and prevalences of schizophrenia and psychotic disorder fluctuated during the 12-month treatment period.
- In the risperidone group, the incidences of extrapyramidal disorder, akathisia, weight increased, headache, and vomiting decreased. However, except for vomiting, the prevalences did not show a similar decrease. The incidences and prevalences of schizophrenia and psychotic disorder fluctuated during the 12-month treatment period.
- A total of 20 (57%) patients in the bifeprunox group and 37 (64%) patients in the risperidone group had one or more newly-emergent adverse events in extension Study 10200. The newly-emergent adverse events seen in ≥4 patients were weight increased (5 patients) and insomnia (4 patients) in the bifeprunox group and extrapyramidal disorder (5 patients), psychotic disorder (4 patients), and schizophrenia (4 patients) in the risperidone group.
- The majority of the patients in the APTSX with adverse events had *mild* or *moderate* events; 24% and 20% of the patients in the bifeprunox and risperidone groups, respectively, had *severe* adverse events. During the 6-month treatment period in extension Study 10200, 17% and 14% of the patients in the bifeprunox and risperidone groups, respectively, had *severe* adverse events. The *severe* adverse events were mostly psychotic disorder and schizophrenia in both treatment groups and both during the 12-month treatment period and during the 6-month extension period.
- In all patients during the 12-month treatment period (APTSX), approximately 75% of the patients in each group had adverse events that were considered to be *related* to IMP by the investigator. In the bifeprunox group, the adverse events that were considered to be *related* to IMP with an incidence ≥15% were vomiting, nausea, and insomnia. In the risperidone group, the adverse events that were considered to be *related* to IMP with an incidence ≥15% were weight increased, akathisia, extrapyramidal disorder, and insomnia.

**Safety Results – Continued**

- During the 6-month treatment period in extension Study 10200 (APTS), 37% of the patients in the bifeprunox group and 52% of the patients in the risperidone group had one or more adverse events that were considered to be *related* to IMP by the investigator. In both treatment groups, the adverse event that were considered to be *related* to IMP with an incidence ≥10% was weight increased.
- In all patients during the 12-month treatment period in lead-in Study 10199 and extension Study 10200 (APTSX), 82 patients, including the 3 patients who died, had 108 SAEs; 47 (29%) patients treated with bifeprunox had 61 SAEs and 35 (20%) patients treated with risperidone had 47 SAEs. Of the 108 SAEs, 24 occurred in extension Study 10200: 7 (20%) patients treated with bifeprunox had 10 SAEs and 10 (17%) patients treated with risperidone had 14 SAEs. The SOC with the highest incidence of SAEs was *psychiatric disorders*.
- The adverse events leading to withdrawal with the highest incidences during the 12-month treatment period as well as during the extension study were schizophrenia and psychotic disorder.
- One patient in the risperidone group committed suicide, 2 patients in the bifeprunox group and 3 patients in the risperidone group attempted suicide, and 4 patients had suicidal ideation (1 patient in the bifeprunox group and 3 patients in the risperidone group).
- Two patients in each treatment group had a syncope or a brief loss of consciousness. Three patients in the bifeprunox group had convulsions.
- During the 12-month treatment period, the incidence of EPS-related adverse events in the risperidone group (40%) was twice that in the bifeprunox group (19%). During the 6-month treatment period in extension Study 10200, the incidence of EPS-related adverse events in the risperidone group (57%) was nearly three times that in the bifeprunox group (20%). In both treatment groups during the 12-month treatment period and during the 6-month treatment period in extension Study 10200, extrapyramidal disorder and akathisia had the highest incidences.
- In both treatment groups, there were minor fluctuations in the SAS, BAS, and AIMS total scores. The mean changes were not clinically relevant, though consistently in favour of bifeprunox for SAS and BAS, and with no clear trend for AIMS.
- In all patients during the 12-month treatment period (APTSX), 14% of the patients in the bifeprunox group and 33% of the patients in the risperidone group started treatment with anticholinergics. This difference between treatment groups in use of anticholinergics was statistically significant ($p < 0.001$). During extension Study 10200, 17% of the patient in the bifeprunox group and 12% of the patients in the risperidone group started treatment with anticholinergics. This difference between treatment groups in use of anticholinergics was not statistically significant.
- The mean changes from baseline in the laboratory tests were small and not clinically relevant.
- At Month 12, 23% of the patients in bifeprunox group and 20% of the patients in the risperidone group had alanine aminotransferase values above the reference range and the mean changes from baseline (entry into lead-in Study 10199) were 5.4 IU/L and 1.5 IU/L in the bifeprunox and risperidone groups, respectively. A total of 3 patients (bifeprunox) had PCS high liver parameters. One of the patients reported the PCS high aspartate aminotransferase (168 IU/L) as a non-serious adverse event (Day 9); the patient, who had a history of seizure, also had a convulsion and a urinary tract infection. The same day, the patient withdrew due to withdrawal of consent and 5 days thereafter, the liver enzyme value had decreased.
- In the bifeprunox group, the total cholesterol, LDL, VLDL, and triglycerides decreased from baseline (entry into lead-in Study 10199) to Months 6 and 12. In the risperidone group, these parameters, except LDL, increased slightly; LDL decreased slightly. In all patients (APTSX), the adjusted mean changes in triglycerides from baseline (entry into lead-in Study 10199) to last assessment were statistically significantly different ($p < 0.001$) between treatment groups: -0.32 mmol/L in the bifeprunox group and 0.11 mmol/L in the risperidone group (LOCF, ANCOVA). In both treatment groups, virtually no mean change was seen in HDL at Month 6 and Month 12.
- In all patients (APTSX), the mean weight change from baseline (entry into lead-in Study 10199) to Month 6 was -2.2 kg in the bifeprunox group and 2.5 kg in the risperidone group.

**Safety Results – Continued**

- In the patients who continued in extension Study 10200 (APTS), the mean weight change from baseline (entry into lead-in Study 10199) to Month 6 was -2.3kg in the bifeprunox group and 3.3kg in the risperidone group. From Months 6 to 12, the mean weight increased in both groups. The mean weight change from baseline (entry into lead-in Study 10199) to Month 12 was -0.4kg in the bifeprunox group and 3.7kg in the risperidone group.
- The adjusted mean weight changes from baseline (entry into lead-in Study 10199) were statistically significantly different ($p < 0.05$) between treatment groups at all time points during the 12-month treatment period (APTSX, OC, ANCOVA), except at Month 12 ($p = 0.63$).
- There were no clinically relevant changes in vital signs, ECG parameters, or physical and neurological examinations.

**Conclusions**

- In this 6-month, double-blind, extension study bifeprunox was safe in the long-term treatment of schizophrenia.
- The high incidence of gastrointestinal symptoms that was seen for bifeprunox in the lead-in study was not seen during continued treatment.
- The adverse events with an incidence of ≥15% in either treatment group during the 12-month treatment period were (bifeprunox *versus* risperidone): insomnia (29% *vs* 32%); vomiting (23% *versus* 10%); nausea (22% *versus* 9%); agitation (17% *versus* 13%); weight decreased (17% *versus* 4%); weight increased (8% *versus* 23%); extrapyramidal disorder (7% *versus* 19%); akathisia (4% *versus* 18%).
- As in the lead-in study, extrapyramidal symptoms were more common during treatment with risperidone than during treatment with bifeprunox.
- The favourable metabolic profile (based on weight changes and blood lipids) seen for bifeprunox compared to risperidone in the lead-in study was also seen during continued treatment.
- During continued treatment, both treatment groups showed improvement from baseline in PANSS total scores, though treatment with bifeprunox was less effective than treatment with risperidone.

**Date of the Report**

12 December 2006

This study was conducted in compliance with the principles of *Good Clinical Practice*.