Supplementary Materials

CLARINET Investigators

Protocol amendments occurring during the study
The protocol was finalised on September 4, 2008, and was subsequently amended as detailed below.

Protocol amendment 1 – March 3, 2009
- Administrative: changes to personnel and contact details
- Assessments: correction of typographical error (clinical laboratory testing was to be performed locally rather than centrally).

Protocol amendment 2 – March 17, 2010
- Administrative: changes to indicate centralisation of Ipsen pharmacovigilance activities in Brisbane, CA, USA (to provide an accessible point of contact in case of emergencies for US centres), and the correction of minor typographical errors.

Protocol amendment 3 – March 28, 2012
- The plan for an interim analysis when all patients had completed the core study, including some new statistical tests of efficacy (to supplement descriptive statistical methods), was included, to support regulatory filing for lanreotide autogel 120 mg in patients with gastroenteropancreatic NETs.
Supplementary methods

Statistical analyses – efficacy

Sensitivity analyses
Two analyses were performed to investigate potential bias in the estimate of the median PFS for lanreotide (main efficacy endpoint): the first assessed the impact on the estimate of patient withdrawals based on investigator-determined PD (despite a central assessment of PD) in the core study (pre-defined analysis); and the second investigated the impact on the estimate of patients with SD at the end of the core study not entering the OLE study (post hoc analysis). In the latter case, patients were assumed to have PD at the first scheduled radiological assessment in the OLE study.

Populations
Efficacy analyses were based on the ITT population (all patients randomly allocated to double-blind treatment in the core study, regardless of participation in the OLE study) or the ITT subset who had PD while receiving placebo and who continued into the OLE study. The exception was a supportive analysis for the main efficacy endpoint, which was based on the per-protocol population (all patients in the ITT population for whom no major protocol violations or deviations occurred during the core study).