United States Post-Marketing Commitments

Name of Product	NDA/BLA Number	Description of Commitment	Date Commitment Given	FDA Projected Completion Date	Commitment Status
Cinryze	BLA 125267	Conduct a clinical trial designed to evaluate higher than labeled dose schedules of CINRYZE for routine prophylaxis of angioedema attacks in patients with Hereditary Angioedema (HAE)	10 Oct 2008	10 Oct 2012	Submitted
Elaprase	BLA 125151	Shire commits to evaluating long-term safety and efficacy data in an observational survey (the Hunter Outcome Survey, HOS) of patients with Hunter syndrome being treated with ELAPRASE. In addition to clinical and laboratory tests that are part of standard medical care for patients with Hunter syndrome, the survey will collect data from patients on the six-minute walk test, from a subset of centers that will have the training and facilities to collect the data in a standardized and reproducible manner, and urinary GAG levels approximately every 6 to 12 months for at least 15 years. Assessments and data collected in the HOS will include those listed in Table 1 of the Hunter Outcome Survey protocol summary version 1.0, dated October 31, 2005, and in the Safety Specification and Pharmacovigilance Plan documented in the ELAPRASE BLA. For pediatric patients in the HOS, data to be collected will include standardized and replicated height, weight, and head circumference measurements in conjunction with deformity assessments and patients method of feeding. The survey will be designed to take advantage of any opportunity to evaluate the effect of ELAPRASE on female reproduction, pregnancy, and lactation. The HOS data will be analyzed at yearly intervals and the results will be submitted in the IND annual reports.	24 Jul 2006	30 Sep 2022	Ongoing

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Elaprase	BLA 125151	BLA 125151/184 PMR#1: To conduct a verification trial to describe clinical benefit attributable to Elaprase (idursulfase) in a cohort of Hunter syndrome patients 5 years of age and younger. At a minimum, this trial will assess longitudinal changes in anthropometric measures (i.e., length/height z-scores, annual growth velocity z-scores, weight zscores) and the progression of skeletal deformities (i.e. joint stiffness, joint contractures) in children being treated with Elaprase (idursulfase). The growth parameters will be followed in these children for a minimum of 5 years from initiation of Elaprase (idursulfase) treatment or until they have reached at least 10 years of age, whichever is longer. The trials will monitor antibody response (binding, neutralizing, and IgE) at least every 6 months. Additionally, the trial will evaluate the relationship between development of immune tolerance and genetic mutations, endogenous enzyme activity level, and anthropometric measures. The trial may be conducted as a separate trial or as a sub-trial under a special protocol within the Hunter	24 Jun 2013	30 Sep 2022	Ongoing
Elaprase	BLA 125151	BLA 125151/184 PMR#3: To develop a validated cross-reactive immunologic material (CRIM) assay for patients with Hunter syndrome and test patient samples in a cohort of patients prior to Elaprase (idursulfase) treatment. Results will be correlated with antibody response (binding, neutralizing and IgE), genetic mutations, enzyme activity level, urinary GAG level, hypersensitivity reactions, and clinical outcome in patients who are receiving Elaprase (idursulfase) treatment. Patients with severe genetic mutations, such as complete deletions or large rearrangements, will be represented in the study. Banked patient samples from other clinical studies may be used.	24 Jun 2013	30 Sep 2019	Ongoing

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Elaprase	BLA 125151	BLA 125151/184 PMR#2: To evaluate a prophylactic immune tolerance regimen in a cohort of Hunter syndrome patients treated with Elaprase (idursulfase) who are at high risk of developing persistent neutralizing antibody that could result in diminished clinical benefit. This immune tolerance regimen will be implemented before or concomitant with onset of therapy. The trial will monitor antibody status (binding, neutralizing, and IgE), urinary GAG, and hypersensitivity reactions in patients at regular intervals. Additionally, the trial will evaluate the relationship between development of immune tolerance and genetic mutations, endogenous enzyme activity level, and clinical outcome. Completion of this PMR is pending the outcome of an Advisory Committee Meeting and completion of PMR 3.	24 Jun 2013	30 Sep 2022	Pending
Gattex/Revestive	NDA 203441	A prospective, multi-center, long-term, observational, registry study, of short bowel syndrome patients treated with teduglutide in a routine clinical setting, to assess the long-term safety of teduglutide. Design the study around a testable hypothesis to rule out a clinically meaningful increase in colorectal cancer risk above an estimated background risk in a suitable comparator. Select and justify the choice of appropriate comparator population(s) and corresponding background rate(s) relative to teduglutide-exposed patients. Provide sample sizes and effect sizes that can be ruled out under various enrollment target scenarios and loss to follow-up assumptions. The study's primary outcome should be colorectal cancer, and secondary outcomes should include other malignancies, colorectal polyps, bowel obstruction, pancreatic and biliary disease, heart failure, and long-term effectiveness. Patients should be enrolled over an initial 5-year period and then followed for a period of at least 10 years from the time of enrollment. Progress updates of registry patient accrual and a demographic summary should be provided annually. Registry safety data should be provided in periodic safety reports.	21 Dec 2012	30 Jun 2031	Ongoing
Kalbitor	125277	Evaluate for cross-reactivity of anti-ecallantide antibodies with TFPI, perform studies to determine if human anti-ecallantide antibodies bind TFPI, and perform suitability studies and epitope mapping of the human anti-ecallantide antibody response if binding is observed.	01 Dec 2009	30 Aug 2010	Submitted

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Kalbitor	125277	Develop and validate anti-ecallantide and anti-P. pastoris-specific human IgE detection assays using a sensitive platform such as ECL. Such assays should be free from interference by anti-ecallantide IgG antibodies.	01 Dec 2009	30 Sep 2010	Submitted
Lialda-Mezavant	NDA 22000	Deferred Pediatric Study under PREA for the treatment of ulcerative colitis in pediatric patients of all ages	16 Jan 2007	30 Nov 2018	Pending
Lialda-Mezavant	NDA 22000	Deferred pediatric study under PREA for the maintenenance of remission of ulcerative colitis in pediatric patients 5 to 17 years of age.	16 Jan 2007	30 Nov 2018	Ongoing
Natpara	BLA 125511	A 26-week randomized, controlled clinical trial to evaluate the longer term safety and effect of an alternative dose(s) and/or dosing regimen(s) of Natpara (parathyroid hormone), including longer term safety with respect to hypercalciuria. This trial should not be initiated until the results from the clinical pharmacology trial (PMR 2856-3) and the nonclinical rat study (PMR 2856-1) have been submitted to and reviewed by the Agency.	23 Jan 2015	31 May 2022	Pending
Natpara	BLA 125511	A study in Fischer 344 rats to ascertain the effect of different Natpara (parathyroid hormone) dosing regimens on osteoblast proliferation, as an indicator of relative osteosarcoma risk.	23 Jan 2015	30 Nov 2016	Pending
Natpara	BLA 125511	An enhanced pharmacovigilance study of osteosarcoma in patients with hypoparathyroidism treated with Natpara (parathyroid hormone). The study will include reports of osteosarcoma for a period of 15 years from the date of approval, and will include assessment and analysis of spontaneous reports of osteosarcoma in patients treated with Natpara (parathyroid hormone), with specialized follow-up to collect additional information on these cases.	23 Jan 2015	20 Sep 2030	Pending
Natpara	BLA 125511	A clinical pharmacology trial to assess the pharmacokinetics (PK) and pharmacodynamic effects (PD) of Natpara (parathyroid hormone) dose and dosing regimen on the control of serum calcium and normalization of calcium excretion in urine. Modeling and simulation using mechanistic model-based assessment of prior PK/PD data should be used to design this trial.	23 Jan 2015	31 May 2018	Delayed
ProAmatine	NDA 19815	Conduct Phase 4 studies to confirm the clinical benefit of midodrine hydrochloride.	06 Sep 1996	31 Mar 2015	Submitted

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Vpriv	NDA 22-575	Shire commits to re-assess the IgE cut point for the current ECL methodology using a chemically synthesized hybrid control. Shire commits to support assay validation using patient baseline values.	24 Feb 2010	31 May 2010	Submitted
Vpriv	NDA 22-575	Shire commits to revise the cut point for the confirmatory anti-velaglucerase and anti-imiglucerase screening assays to a level that is less than or equal to the cut point of the screening assay.	26 Feb 2010	31 May 2010	Submitted
Vpriv	NDA 22-575	Shire commits to utilize an antibody screening cut point based on a mean + 1.645 standard deviation for assay values from treatment naïve Gaucher patients. Shire will utilize the same methodology to calculate the anti-imiglucerase ECL cut point.	26 Feb 2010	31 May 2010	Submitted
Vpriv	NDA 22-575	Shire commits to develop an assay to measure the ability of patient antibodies to block the uptake of velaglucerase and imiglucerase into target cells.	26 Feb 2010	30 Nov 2010	Submitted
Vyvanse	NDA 21,977	A controlled trial to evaluate the longer-term (i.e., maintenance) efficacy of lisdexamfetamine in the treatment of adults with binge eating disorder. This trial must be placebo-controlled, utilize a randomized withdrawal design, and include an adequate period of stabilization with open-label treatment of lisdexamfetamine prior to double-blind randomization.	30 Jan 2015	28 Feb 2018	Pending