



## United States Post-Marketing Commitments

Name of Product	NDA/BLA Number	Description of Commitment	Date		
			Commitment Given	FDA Projected Completion Date	Commitment Status
Adynovate/Adynovi	125566	Deferred pediatric study under PREA for routine prophylaxis to compare the efficacy and safety of two different pharmacokinetics (PK) guided dosing regimens in pediatric patients ages 12 to less than 17 years (A phase	13-Nov-2015	30-Sep-2019	Ongoing
Adynovate/Adynovi	125566	Conduct "A phase 3, prospective, randomized, multi-center clinical study comparing the safety and efficacy of BAX 855 [ADYNOVATE] following PK-guided prophylaxis targeting two different FVIII trough levels in subjects with severe Hemophilia A" [clinical study 261303] – ADULT COMPONENT ONLY.	13-Nov-2015	30-Sep-2019	Pending
Adynovate/Adynovi	125566	Conduct "A phase 3, prospective, open label, multi-center study of efficacy and safety of ADYNOVATE in the perioperative management of bleeding in PTPs age 2-75 years" [clinical study 261204] – ADULT COMPONENT ONLY.	13-Nov-2015	31-Dec-2017	Submitted
Adynovate/Adynovi	125566	Conduct "A phase 3b, prospective, open label, and multicenter continuation study of safety and efficacy of ADYNOVATE in the routine prophylaxis of bleeding to reduce the frequency of bleeding episodes in PTPs" age 12 years and above [clinical study 261302].	13-Nov-2015	30-Sep-2018	Submitted
Adynovate/Adynovi	125566	Conduct "A phase 3, multi-center, open label study to investigate safety and immunogenicity of ADYNOVATE in previously untreated patients(PUPs)" [clinical study 261203]. This study will evaluate on-demand treatment and control of bleeding episodes in the setting of routine prophylaxis to reduce the frequency of bleeding episodes, as well as the perioperative management of bleeding.	13-Nov-2015	30-Sep-2023	Delayed

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Aralast NP	125039	Contingent on the outcome of the pilot trial described in commitment 3, conduct and report the results of an adequately-powered study of clinically meaningful endpoints(s). Based on the results of the pilot study and the available scientific data at the time that this study is being designed, work with entities maintaining registries of alpha1-proteinase inhibitor deficient patients and with the National Institutes of Health (NIH) to design and conduct an adequately-powered study of a clinically meaningful endpoint(s). The study design could involve a single product or could potentially involve a cooperative simultaneous study of multiple products in parallel arms, using a factorial design.	23-Dec-2002	31-Jul-2024	Pending
Aralast NP	125039	Conduct and report the results of a pilot trial to determine the effect of regular administration of the product on one or more clinically meaningful endpoint(s). Examples of acceptable endpoints include pulmonary exacerbations, serial pulmonary functions, and serial quantitative computerized axial tomographic (CT) lung scans.	23-Dec-2002	31-Jul-2017	Delayed
Cinryze	BL 125267	ViroPharma will re-test the available samples retained from Phase 3 Study (Protocol 0624-301) with the new immunogenicity assay and will submit the results of the study in a "Postmarketing Submission - Final Study Report" by January 1, 2020.	18-Jun-2018	1-Jan-2020	Pending

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Elaprase	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 Outcome Survey.	24-Jun-2013	30-Sep-2022	Ongoing
Elaprase	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	31-Jan-2017	Delayed

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Elaprase	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

Name of Product	NDA/BLA Number	Description of Commitment	Date Commitment Given	FDA Projected Completion Date	Commitment Status
Elaprase	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
HyQvia	125402	Baxter commits to conducting an evaluation of long-term safety study of HYQVIA in 250 patients with PID including up to 50 patients developing antibodies. The duration of the study is 6 years and subjects who become antibody positive will be eligible for further long term safety evaluation and antibody characterization.	12-Sep-2014	12-Nov-2021	Ongoing
HyQvia	125402	Baxter commits to establish and maintain a pregnancy registry to assess a) the course and outcome of the pregnancy, b) the development of the fetus/infant at birth, and c) the development of the infant for two years following birth. The duration of the registry will be six years and will be open to all women who become pregnant while taking HYQVIA.	12-Sep-2014	12-Nov-2021	Ongoing

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HyQvia	125402	Deferred pediatric study under PREA for the treatment of primary immunodeficiency in pediatric patients 2-16 years of age.	12-Sep-2014	31-Jul-2027	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.	1-Dec-2009	30-Sep-2010	Submitted
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.	1-Dec-2009	30-Sep-2010	Submitted
Lialda/Mezavant	N022000	Deferred Pediatric Study under PREA for the treatment of ulcerative colitis in pediatric patients of all ages	16-Jan-2007	30-Nov-2018	Ongoing
Lialda/Mezavant	N022000	Deferred pediatric study under PREA for the maintenance of remission of ulcerative colitis in pediatric patients 5 to 17 years of age.	16-Jan-2007	30-Nov-2018	Ongoing
Mydayis	22063	A single-dose, open-label, randomized pharmacokinetic study of MYDAYIS (mixed salts of a single-entity amphetamine product) extended-release in male and female children (4 to less than 6 years of age) with ADHD.	20-Jun-2017	30-Jun-2019	Pending
Mydayis	22063	A 4-week randomized, double-blind, placebo-controlled, fixed -dose study of MYDAYIS (mixed salts of a single-entity amphetamine product) extended release 6.25 mg in 4 to 5 year olds diagnosed with ADHD.	20-Jun-2017	30-Jun-2019	Released
Mydayis	22063	A one year Pediatric Open-Label Safety Study for patients age 4 to 12 years (at the time of entry into PMR 3224-1, PMR 3224-2, or PMR 3224-3) with ADHD.	20-Jun-2017	30-Jun-2020	Ongoing
Mydayis	22063	Conduct a 4-week randomized, double-blind, placebo-controlled, fixed-dose efficacy and safety study of MYDAYIS (mixed salts of a single-entity amphetamine extended release) 6.25mg in 6 to 12 year-olds diagnosed with ADHD. (Study SHP465-309)	20-Jun-2017	30-Jun-2019	Pending

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Natpara	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-Mar-2017	Delayed
Natpara	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	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	30-Sep-2030	Ongoing
Obizur	125512	To collect additional efficacy and safety data for OBIZUR in adults with acquired hemophilia A in the Treatment Registry study under Protocol 241302, "A Non-Interventional Study of Safety and Effectiveness of Recombinant Porcine Sequence FVIII (OBIZUR) in the Treatment of Bleeding Episodes for Patients with Acquired Hemophilia A."	23-Oct-2014	31-Jan-2020	Ongoing

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Oncaspar	103411	To commit to providing complete validation data for the anti-Oncaspar ELISA assay. The validation studies will provide an assessment of the sensitivity (in mass units of antibodies), specificity, and reproducibility of the assay. The cutpoint for the assay (the value that discriminates positive samples from negative samples) will be determined by using samples from unexposed patients and validated positive controls. This cut point value will be used to determine the number and percent of patients who develop antibodies to Oncaspar during clinical trials. The assay validation will be performed with insight obtained from Mire-Sluis et al. J. of Immunol. Methods, 2004, 289: 1-16.	1-Feb-1994	31-Jan-2007	Submitted
Oncaspar	103411	To commit to development and validation of an assay to detect the presence of neutralizing antibodies to Oncaspar. Validation studies will provide an assessment of the sensitivity (in mass units of antibodies), specificity, and reproducibility of the assay. The cutpoint for the assay (the value that discriminates positive samples from negative samples) will be determined by using samples from unexposed patients and validated positive controls. This value will be used to determine the number and percent of patients who develop neutralizing antibodies to the Oncaspar during clinical trials.	1-Feb-1994	31-Jan-2007	Submitted
Proamatine	19815	Conduct Phase 4 studies to confirm the clinical benefit of midodrine hydrochloride.	6-Sep-1996	15-Mar-2015	Submitted

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Revestive/Gattex	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
Rixubis	125446	Evaluation of long-term efficacy and safety of RIXUBIS in 100 patients of all age groups with hemophilia B, of which at least 25 will be subjects naïve to RIXUBIS.	26-Jun-2013	30-Jun-2016	Delayed
Vyvanse/Elvanse - Chewable tablet	208-510	Deferred pediatric study under PREA in children ages 4 to less than 6 years with a diagnosis of ADHD to obtain pharmacokinetic, safety, and tolerability data to inform dose selection for efficacy and safety studies in pediatric patients with ADHD.	28-Jan-2017	30-Jun-2019	Ongoing
Vyvanse/Elvanse - Chewable tablet	208-510	A randomized, double-blind, placebo-controlled efficacy study of VYVANSE (lisdexamfetamine dimesylate) chewable tablets in children ages 4 to less than 6 years diagnosed with ADHD.	28-Jan-2017	30-Jun-2023	Pending
Vyvanse/Elvanse - Chewable tablet	208-510	A 12-month open-label safety study of patients age 4 to less than 6 years (at the time of entry into PMR 3149-1 or PMR 3149-2, or at the time of enrollment if directly enrolled into PMR 3149-3) diagnosed with ADHD treated with VYVANSE (lisdexamfetamine dimesylate) chewable tablets.	28-Jan-2017	30-Jun-2023	Ongoing