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(54) **Title:** USE OF GABOXADOL IN THE TREATMENT OF GASTROINTESTINAL TRACT DISORDERS AND ASTHMA

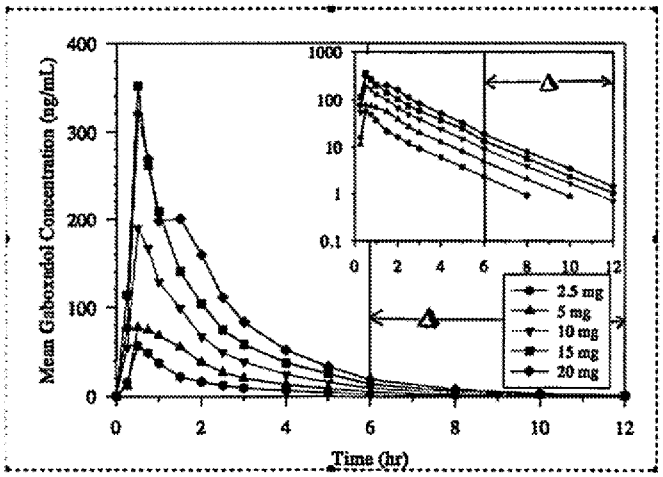

FIG. 1

(57) **Abstract:** Treatment of irritable bowel syndrome, Crohn's disease, celiac disease, ulcerative colitis, microscopic colitis, and asthma using gaboxadol or a pharmaceutically acceptable salt thereof is provided. Also provided are therapeutic compositions that may be used to improve one or more symptoms of irritable bowel syndrome, Crohn's disease, celiac disease, ulcerative colitis, microscopic colitis, or asthma.

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USE OF GABOXADOL IN THE TREATMENT OF GASTROINTESTINAL TRACT DISORDERS AND ASTHMA

TECHNICAL FIELD

[0001] Methods of treating gastrointestinal tract disorders and asthma.

BACKGROUND

[0002] Gastrointestinal tract disorders include irritable bowel syndrome (IBS), Crohn's disease, celiac disease, ulcerative colitis and microscopic colitis. According to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), IBS is a group of symptoms that occur together, including cramping, repeated abdominal pain, bloating, and changes in bowel movements which may be diarrhea, constipation, or both. These symptoms may occur without any visible signs of damage or disease in the digestive tract. IBS is classified into three types, 1) IBS with constipation (IBS-C), 2) IBS with diarrhea (IBS-D), and 3) IBS with mixed bowel habits (IBS-M). The cause or causes of IBS are not clear. Certain cases of IBS may be triggered by infection, referred to as post-infectious IBS. Changes in diet, lifestyle changes, probiotics, mental health therapy and medications are used to treat IBS. Anti-diarrheal medications such as loperamide are used to treat IBS-D. Fiber supplements and laxatives, e.g., lubipostone, are used to treat IBS-C. Antispasmodics such as dicyclomine or peppermint oil, and antidepressants, e.g., tricyclics, SSRIs, may be used to treat overall symptoms, cramps and abdominal pain associated with IBS. There is a continuing need for effective therapies to treat IBS.

[0003] According to the NIDDK, Crohn's disease is an inflammatory bowel disease that most commonly effects the small intestine and the beginning of the large intestine. However, it can affect any part of the digestive tract such as the mouth, esophagus, stomach and anus. The cause or causes of Crohn's disease are unclear. It may be genetic in some instances. In certain cases, it may be an autoimmune reaction which causes inflammation. Other possible causes are cigarette smoking, nonsteroidal anti-inflammatory drugs, antibiotics and oral contraceptives. A high fat diet may also contribute to development of Crohn's disease. Symptoms of Crohn's disease include, diarrhea, cramping, abdominal pain, anemia, fever and nausea. Complications arising from Crohn's disease include intestinal obstructions, fistulas, abscesses, anal fissures, ulcers, malnutrition and inflammation in other parts of the body. No single treatment works for all cases of Crohn's disease. Changes in diet and

medications may be used to treat Crohn's disease. Medications include aminosalicylates which can reduce inflammation, corticosteroids which reduce the activity of the immune system and reduce inflammation, and immunomodulators which reduce immune system activity. Monoclonal antibodies have also been used to reduce the activity of the immune system, thus reducing inflammation. The foregoing medications may be associated with serious side effects. There is a continuing need for effective therapies to treat Crohn's disease.

[0004] According to the NIDDK, celiac disease is a digestive disorder that damages the small intestine. It is triggered by ingestion of foods containing gluten, a protein found, e.g., in wheat, barley and rye, which causes an autoimmune reaction. Celiac disease appears to be genetic in nature. Symptoms are more common in children and include bloating, chronic diarrhea, constipation, gas, nausea, pale, foul smelling stools, stomach pain and malabsorption of nutrients which can cause damage to teeth enamel, delayed puberty, failure to thrive in infants, slowed growth and weight loss. Adults are less likely to have digestive symptoms, but may exhibit anemia, red, shiny tongue, bone or joint pain, depression, headaches, dermatitis herpetiformis, infertility, canker sores, seizures, fatigue and weak, brittle bones. Adult gastrointestinal (GI) symptoms include abdominal pain, bloating, intestinal blockage, ulcers on the stomach or intestinal lining. Treatment typically involves avoidance of gluten containing foods. There is a continuing need for effective therapies to reduce or eliminate symptoms of celiac disease.

[0005] According to the NIDDK, ulcerative colitis is a chronic disease that causes inflammation and ulcers on the inner lining of the large intestine. Ulcerative colitis most often begins gradually and can become worse over time. Symptoms can be mild to severe. Most people have periods of remission—times when symptoms disappear—that can last for weeks or years. The goal of care is to keep people in remission long term. The exact cause of ulcerative colitis is unknown. The following factors may play a role in causing ulcerative colitis: genetic predisposition, an abnormal immune reaction targeting the inner lining of the intestine, nonsteroidal anti-inflammatory drugs, antibiotics and oral contraceptives. Symptoms include urgent need to have a bowel movement, fatigue, nausea, loss of appetite, weight loss, fever, anemia, joint pain, and rashes. About 10 percent of people can have severe symptoms, such as frequent, bloody bowel movements; fevers; and severe abdominal cramping. Treatment of ulcerative colitis symptoms typically involves medications such as aminosalicylates which can reduce inflammation, corticosteroids which reduce the activity of the immune system and reduce inflammation, and immunomodulators which reduce immune

system activity. Monoclonal antibodies have also been used to reduce the activity of the immune system, thus reducing inflammation. The foregoing medications may be associated with serious side effects. There is a continuing need for effective therapies to treat ulcerative colitis.

[0006] According to the NIDDK, microscopic colitis is an inflammation that can only be seen with a microscope. The two types of microscopic colitis are collagenous colitis and lymphocytic colitis. In both types of microscopic colitis, an increase in the number of lymphocytes can be seen in the epithelium of the colon. The two types of colitis affect the colon tissue in slightly different ways. In lymphocytic colitis the number of lymphocytes is higher, and the tissues and lining of the colon are of normal thickness. In collagenous colitis the layer of collagen underneath the epithelium builds up and becomes thicker than normal. Although the exact cause of microscopic colitis is unknown, it is believed that it may result from an abnormal immune response to bacteria that normally live in the colon. Several other factors may play a role in causing microscopic colitis, including autoimmune diseases, medications, infections, genetic factors and bile acid malabsorption. The most common symptom of microscopic colitis is chronic, watery, non-bloody diarrhea. Episodes of diarrhea can last for weeks, months, or even years. However, many people with microscopic colitis may have long periods without diarrhea. Other signs and symptoms of microscopic colitis can include a strong urgency to have a bowel movement or a need to go to the bathroom quickly, pain, cramping, or bloating in the abdomen that is usually mild, weight loss, nausea, fecal incontinence, i.e., accidental passing of stool or fluid from the rectum, especially at night, and dehydration that results from not taking in enough liquids to replace fluids lost through diarrhea. Treatment of ulcerative colitis symptoms typically involves medications such as antidiarrheals such as bismuth subsalicylate, diphenoxylate/atropine and loperamide, corticosteroids such as budesonide and prednisone, anti-inflammatory medications such as mesalamine and sulfasalazine, cholestyramine resin—a medication that blocks bile acids, antibiotics such as metronidazole and erythromycin, immunomodulators such as mercaptopurine , azathioprine and methotrexate, and anti-TNF therapies such as infliximab and adalimumab. Some of the foregoing medications may be associated with serious side effects. There is a continuing need for effective therapies to treat microscopic colitis.

[0007] According to the National Heart, Lung and Blood Institute (NHLBI) asthma is a chronic lung disease that inflames and narrows the airways. When the airways react, the muscles around them tighten. This narrows the airways, causing less air to flow into the lungs. The swelling also can worsen, making the airways even narrower. This chain reaction

can result in asthma symptoms. Asthma causes recurring periods of wheezing, chest tightness, shortness of breath, and coughing. Symptoms can happen each time the airways are inflamed. Asthma affects people of all ages, but it most often starts during childhood. In the United States, more than 25 million people are known to have asthma. About 7 million of these people are children. The exact cause of asthma isn't known. Asthma is a long-term disease that has no cure. The goal of asthma treatment is to control the disease. Most people who have asthma need to take long-term control medicines daily to help prevent symptoms. Inhaled corticosteroids are the preferred medicine for long-term control of asthma. Other long-term control medicines include anti-inflammatory medicines, such as cromolyn, immunomodulators, such as omalizumab (anti-IgE), inhaled long-acting beta2-agonists, leukotriene modifiers, and theophylline. Some of the foregoing medications may be associated with serious side effects. There is a continuing need for effective therapies to treat asthma.

[0008] Gaboxadol (4,5,6,7-tetrahydroisoxazolo [5,4-c]pyridine-3-ol) (THIP)) is described in EP Patent No. 0000338 and in EP Patent No. 0840601, U.S. Patent Nos. 4,278,676, 4,362,731, 4,353,910, and WO 2005/094820. Gaboxadol is a selective $GABA_A$ receptor agonist with a preference for δ-subunit containing $GABA_A$ receptors. In the early 1980s gaboxadol was the subject of a series of pilot studies that tested its efficacy as an analgesic and anxiolytic, as well as a treatment for tardive dyskinesia, Huntington's disease, Alzheimer's disease, and spasticity. In the 1990s gaboxadol moved into late stage development for the treatment of insomnia. The development was discontinued after the compound failed to show significant effects in sleep onset and sleep maintenance in a three-month efficacy study. Additionally, patients with a history of drug abuse who received gaboxadol experienced a steep increase in psychiatric adverse events.

SUMMARY

[0009] Methods of treating irritable bowel syndrome described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in irritable bowel syndrome. Methods of treating irritable bowel syndrome described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in one or more symptoms of irritable bowel syndrome. Methods of treating irritable bowel syndrome

described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in irritable bowel syndrome the next day. Methods of treating irritable bowel syndrome described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in the patient for more than 6 hours after administration to the patient. Methods of treating irritable bowel syndrome are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile including a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating irritable bowel syndrome are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating irritable bowel syndrome are described herein which include administering to a patient in need thereof a first pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile comprising a mean $AUC_{0-\infty}$ of at least 20% less than the first pharmaceutical composition. Methods of treating irritable bowel syndrome are described herein which include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof in combination with a medicament selected from the group consisting of anti-diarrheal, anti-spasmodic and antidepressant wherein the method provides improvement in irritable bowel syndrome.

[0010] Methods of treating Crohn's disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in Crohn's disease. Methods of treating Crohn's disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in one or more symptoms of Crohn's

disease. Methods of treating Crohn's disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in Crohn's disease the next day. Methods of treating Crohn's disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in the patient for more than 6 hours after administration to the patient. Methods of treating Crohn's disease are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile including a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating Crohn's disease are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating Crohn's disease are described herein which include administering to a patient in need thereof a first pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile comprising a mean $AUC_{0-\infty}$ of at least 20% less than the first pharmaceutical composition. Methods of treating Crohn's disease are described herein which include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof in combination with a medicament selected from the group consisting of anti-diarrheal, anti-spasmodic, aminosalicylate, corticosteroid, immunomodulator and antidepressant, wherein the method provides improvement in Crohn's disease.

[0011] Methods of treating celiac disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in celiac disease. Methods of treating celiac disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in one or more symptoms of celiac disease. Methods of

treating celiac disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in celiac disease the next day. Methods of treating celiac disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in the patient for more than 6 hours after administration to the patient. Methods of treating celiac disease are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile including a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating celiac disease are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating celiac disease are described herein which include administering to a patient in need thereof a first pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile comprising a mean $AUC_{0-\infty}$ of at least 20% less than the first pharmaceutical composition. Methods of treating celiac disease are described herein which include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof in combination with a medicament selected from the group consisting of anti-diarrheal, anti-spasmodic and antidepressant wherein the method provides improvement in celiac disease.

[0012] Methods of treating ulcerative colitis described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in ulcerative colitis. Methods of treating ulcerative colitis se described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in one or more symptoms of ulcerative colitis. Methods of treating ulcerative colitis described herein include administering to a

patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in ulcerative colitis the next day. Methods of treating ulcerative colitis described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in the patient for more than 6 hours after administration to the patient. Methods of treating ulcerative colitis are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile including a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating ulcerative colitis are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating ulcerative colitis are described herein which include administering to a patient in need thereof a first pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile comprising a mean $AUC_{0-\infty}$ of at least 20% less than the first pharmaceutical composition. Methods of treating ulcerative colitis are described herein which include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof in combination with a medicament selected from the group consisting of anti-diarrheal, anti-spasmodic, aminosalicylate, corticosteroid, immunomodulator and antidepressant wherein the method provides improvement in ulcerative colitis.

[0013] Methods of treating microscopic colitis described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in microscopic colitis. Methods of treating microscopic colitis se described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in one or more symptoms of

microscopic colitis. Methods of treating microscopic colitis described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in microscopic colitis the next day. Methods of treating microscopic colitis described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in the patient for more than 6 hours after administration to the patient. Methods of treating microscopic colitis are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile including a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating microscopic colitis are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating microscopic colitis are described herein which include administering to a patient in need thereof a first pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile comprising a mean $AUC_{0-\infty}$ of at least 20% less than the first pharmaceutical composition. Methods of treating microscopic colitis are described herein which include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof in combination with a medicament selected from the group consisting of anti-diarrheal, anti-spasmodic, aminosalicylate, corticosteroid, immunomodulator and antidepressant wherein the method provides improvement in microscopic colitis.

[0014] Methods of treating asthma described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in asthma. Methods of treating asthma described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides

improvement in one or more symptoms of asthma. Methods of treating asthma described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in asthma the next day. Methods of treating asthma described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in the patient for more than 6 hours after administration to the patient. Methods of treating asthma are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile including a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating asthma are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating asthma are described herein which include administering to a patient in need thereof a first pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile comprising a mean $AUC_{0-\infty}$ of at least 20% less than the first pharmaceutical composition. Methods of treating asthma are described herein which include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof in combination with a medicament selected from the group consisting of anti-inflammatory, immunomodulator, long-acting beta2-agonist, leukotriene modifier and theophylline wherein the method provides improvement in asthma.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] FIG. 1 shows the arithmetic mean plasma concentration-time profiles of gaboxadol following single oral doses (2.5, 5, 10, 15, and 20 mg) as described in Example 1 with horizontal lines Δ indicating the change between 6 and 12 hours.

[0016] FIG. 2 shows the arithmetic mean plasma concentration-time profiles of gaboxadol following single oral doses (2.5, 5, 10, 15, and 20 mg) as described in Example 1.

DETAILED DESCRIPTION

[0017] Described herein are methods of treating irritable bowel syndrome with gaboxadol or a pharmaceutically acceptable salt thereof. As used herein, "irritable bowel syndrome" includes IBS-C, IBS-D, and IBS-M. Also described herein are methods of treating Crohn's disease with gaboxadol or a pharmaceutically acceptable salt thereof. Also described herein are methods of treating celiac disease with gaboxadol or a pharmaceutically acceptable salt thereof. Also described herein are methods of treating ulcerative colitis with gaboxadol or a pharmaceutically acceptable salt thereof. Also described herein are methods of treating microscopic colitis with gaboxadol or a pharmaceutically acceptable salt thereof. As used herein, "microscopic colitis" includes collagenous colitis and lymphocytic colitis. Also described herein are methods of treating asthma with gaboxadol or a pharmaceutically acceptable salt thereof.

[0018] Many pharmaceutical products are administered as a fixed dose, at regular intervals, to achieve therapeutic efficacy. Its duration of action is reflected by its plasma half-life. Gaboxadol is a selective $GABA_A$ receptor agonist with a relatively short half-life ($t_{1/2}$ = 1.5 h). Since efficacy is often dependent on sufficient exposure within the central nervous system administration of CNS drugs with a short half-life may require frequent maintenance dosing.

[0019] Advantageously disclosed herein are methods of treating IBS by administration of gaboxadol or a pharmaceutically acceptable salt thereof. For example, in embodiments, methods of treating IBS are provided which include administering to a patient in need thereof a pharmaceutical composition including about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement for more than 6 hours after administration to the patient.

[0020] Advantageously disclosed herein are methods of treating Crohn's disease by administration of gaboxadol or a pharmaceutically acceptable salt thereof. For example, in embodiments, methods of treating Crohn's disease are provided which include administering to a patient in need thereof a pharmaceutical composition including about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement for more than 6 hours after administration to the patient.

[0021] Advantageously disclosed herein are methods of treating ulcerative colitis by administration of gaboxadol or a pharmaceutically acceptable salt thereof. For example, in embodiments, methods of treating ulcerative colitis are provided which include administering to a patient in need thereof a pharmaceutical composition including about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement for more than 6 hours after administration to the patient.

[0022] Advantageously disclosed herein are methods of treating celiac disease by administration of gaboxadol or a pharmaceutically acceptable salt thereof. For example, in embodiments, methods of treating celiac disease with are provided which include administering to a patient in need thereof a pharmaceutical composition including about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement for more than 6 hours after administration to the patient.

[0023] Advantageously disclosed herein are methods of treating microscopic colitis with by administration of gaboxadol or a pharmaceutically acceptable salt thereof. For example, in embodiments, methods of treating microscopic colitis are provided which include administering to a patient in need thereof a pharmaceutical composition including about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement for more than 6 hours after administration to the patient.

[0024] Advantageously disclosed herein are methods of treating asthma with by administration of gaboxadol or a pharmaceutically acceptable salt thereof. For example, in embodiments, methods of treating asthma with are provided which include administering to a patient in need thereof a pharmaceutical composition including about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement for more than 6 hours after administration to the patient.

[0025] Methods of treating IBS described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in one or more symptoms of IBS. Methods of treating IBS described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in IBS the next day. Methods of treating IBS described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in the patient for more than 6 hours after administration to the patient. Methods of treating IBS are described herein which include administering to a patient in need thereof

gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile including a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating IBS are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating IBS are described herein which include administering to a patient in need thereof a first pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile comprising a mean $AUC_{0-\infty}$ of at least 20% less than the first pharmaceutical composition.

[0026] Methods of treating Crohn's disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in one or more symptoms of Crohn's disease. Methods of treating Crohn's disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in Crohn's disease the next day. Methods of treating Crohn's disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in the patient for more than 6 hours after administration to the patient. Methods of treating Crohn's disease are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile including a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating Crohn's disease are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng ng•hr/ml and wherein the method

provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating Crohn's disease are described herein which include administering to a patient in need thereof a first pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile comprising a mean $AUC_{0-\infty}$ of at least 20% less than the first pharmaceutical composition.

[0027] Methods of treating celiac disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in one or more symptoms of celiac disease. Methods of treating celiac disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in celiac disease the next day. Methods of treating celiac disease described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in the patient for more than 6 hours after administration to the patient. Methods of treating celiac disease are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile including a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating celiac disease are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating celiac disease are described herein which include administering to a patient in need thereof a first pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile comprising a mean $AUC_{0-\infty}$ of at least 20% less than the first pharmaceutical composition.

[0028] Methods of treating ulcerative colitis described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in one or more symptoms of ulcerative colitis. Methods of treating ulcerative colitis described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in ulcerative colitis the next day. Methods of treating ulcerative colitis described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in the patient for more than 6 hours after administration to the patient. Methods of treating ulcerative colitis are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile including a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating ulcerative colitis are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating ulcerative colitis are described herein which include administering to a patient in need thereof a first pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile comprising a mean $AUC_{0-\infty}$ of at least 20% less than the first pharmaceutical composition.

[0029] Methods of treating microscopic colitis described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in one or more symptoms of microscopic colitis. Methods of treating microscopic colitis described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in microscopic colitis the next day. Methods of treating microscopic colitis described herein

include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in the patient for more than 6 hours after administration to the patient. Methods of treating microscopic colitis are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile including a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating microscopic colitis are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating microscopic colitis are described herein which include administering to a patient in need thereof a first pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile comprising a mean $AUC_{0-\infty}$ of at least 20% less than the first pharmaceutical composition.

[0030] Methods of treating asthma described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in one or more symptoms of asthma. Methods of treating asthma described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in asthma the next day. Methods of treating asthma described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in the patient for more than 6 hours after administration to the patient. Methods of treating asthma are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile including a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of

treating asthma are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. Methods of treating asthma are described herein which include administering to a patient in need thereof a first pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition comprising gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile comprising a mean $AUC_{0-\infty}$ of at least 20% less than the first pharmaceutical composition.

[0031] Embodiments described herein provide that a patient in need thereof is administered a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof. Gaboxadol or pharmaceutically acceptable salt thereof may be provided as an acid addition salt, a zwitter ion hydrate, zwitter ion anhydrate, hydrochloride or hydrobromide salt, or in the form of the zwitter ion monohydrate. Acid addition salts, include but are not limited to, maleic, fumaric, benzoic, ascorbic, succinic, oxalic, bis-methylenesalicylic, methanesulfonic, ethane-disulfonic, acetic, propionic, tartaric, salicylic, citric, gluconic, lactic, malic, mandelic, cinnamic, citraconic, aspartic, stearic, palmitic, itaconic, glycolic, p-amino-benzoic, glutamic, benzene sulfonic or theophylline acetic acid addition salts, as well as the 8-halotheophyllines, for example 8-bromo-theophylline. In other suitable embodiments, inorganic acid addition salts, including but not limited to, hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric or nitric acid addition salts may be used.

[0032] In embodiments, gaboxadol is provided as gaboxadol monohydrate. One skilled in the art will readily understand that the amounts of active ingredient in a pharmaceutical composition will depend on the form of gaboxadol provided. For example, pharmaceutical compositions of including 5.0, 10.0, or 15.0 mg gaboxadol correspond to 5.6, 11.3, or 16.9 mg gaboxadol monohydrate.

[0033] In embodiments, gaboxadol is crystalline, such as the crystalline hydrochloric acid salt, the crystalline hydrobromic acid salt, or the crystalline zwitter ion monohydrate. In embodiments, gaboxadol is provided as a crystalline monohydrate.

[0034] Deuteration of pharmaceuticals to improve pharmacokinetics (PK), pharmacodynamics (PD), and toxicity profiles, has been demonstrated previously with some

classes of drugs. Accordingly the use of deuterium enriched gaboxadol is contemplated and within the scope of the methods and compositions described herein. Deuterium can be incorporated in any position in replace of hydrogen synthetically, according to the synthetic procedures known in the art. For example, deuterium may be incorporated to various positions having an exchangeable proton, such as the amine N--H, via proton-deuterium equilibrium exchange. Thus, deuterium may be incorporated selectively or non-selectively through methods known in the art to provide deuterium enriched gaboxadol. *See* Journal of Labeled Compounds and Radiopharmaceuticals 19(5) 689-702 (1982).

[0035] Deuterium enriched gaboxadol may be described by the percentage of incorporation of deuterium at a given position in the molecule in the place of hydrogen. For example, deuterium enrichment of 1% at a given position means that 1% of molecules in a given sample contain deuterium at that specified position. The deuterium enrichment can be determined using conventional analytical methods, such as mass spectrometry and nuclear magnetic resonance spectroscopy. In embodiments deuterium enriched gaboxadol means that the specified position is enriched with deuterium above the naturally occurring distribution (*i.e.*, above about.0156%). In embodiments deuterium enrichment is no less than about 1%, no less than about 5%, no less than about 10%, no less than about 20%, no less than about 50%, no less than about 70%, no less than about 80%, no less than about 90%, or no less than about 98% of deuterium at a specified position.

[0036] In embodiments, methods of treating IBS include administering to a patient in need thereof a pharmaceutical composition including about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof. In embodiments, methods of treating Crohn's disease include administering to a patient in need thereof a pharmaceutical composition including about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof. In embodiments, methods of treating ulcerative colitis include administering to a patient in need thereof a pharmaceutical composition including about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof. In embodiments, methods of treating celiac disease include administering to a patient in need thereof a pharmaceutical composition including about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof. In embodiments, methods of treating microscopic colitis include administering to a patient in need thereof a pharmaceutical composition including about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof. In embodiments, methods of treating asthma include administering to a patient in need thereof a pharmaceutical composition

including about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof.

[0037] In embodiments, the pharmaceutical compositions include 0.1 mg to 25 mg, 0.1 mg to 20 mg, 0.1 mg to 15 mg, 0.5 mg to 25 mg, 0.5 mg to 20 mg, 0.5 to 15 mg, 1 mg to 25 mg, 1 mg to 20 mg, 1 mg to 15 mg, 1.5 mg to 25 mg, 1.5 mg to 20 mg, 1.5 mg to 15 mg, 2 mg to 25 mg, 2 mg to 20 mg, 2 mg to 15 mg, 2.5 mg to 25 mg, 2.5 mg to 20 mg, 2.5 mg to 15 mg, 3 mg to 25 mg, 3 mg to 20 mg, 3 mg to 15 mg gaboxadol or a pharmaceutically acceptable salt thereof.

[0038] In embodiments, the pharmaceutical compositions include 5 mg to 20 mg, 5 mg to 10 mg, 4 mg to 6 mg, 6 mg to 8 mg, 8 mg to 10 mg, 10 mg to 12 mg, 12 mg to 14 mg, 14 mg to 16 mg, 16 mg to 18 mg, or 18 mg to 20 mg gaboxadol or a pharmaceutically acceptable salt thereof.

[0039] In embodiments, the pharmaceutical compositions include 0.1 mg, 0.25 mg, 0.5 mg, 1 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 7 mg, 7.5 mg, 8 mg, 8.5 mg, 9 mg, 9.5 mg,10 mg, 10.5 mg, 11 mg, 12 mg, 12.5 mg, 13 mg, 14 mg, 15 mg, 16 mg, 17 mg, 17.5 mg, 18 mg, 19 mg, 20 mg, 21 mg, 22 mg, 23 mg, 24 mg, 25 mg, 26 mg, 27 mg, 28 mg, 29 mg, or 30 mg gaboxadol or a pharmaceutically acceptable salt thereof or amounts that are multiples of such doses. In embodiments, the pharmaceutical compositions include 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, or 20 mg gaboxadol or a pharmaceutically acceptable salt thereof.

[0040] In embodiments, pharmaceutical compositions herein may be provided in the form of tablets, capsules, suppositories, inhalants, solutions, suspensions or emulsions. In embodiments, pharmaceutical compositions herein are suitable for parenteral administration, including, *e.g.*, intramuscularly (i.m.), intravenously (i.v.), subcutaneously (s.c.), intraperitoneally (i.p.), or intrathecally (i.t.). The parenteral compositions herein must be sterile for administration by injection, infusion or implantation into the body and may be packaged in either single-dose or multi-dose containers. The parenteral compositions may be contained in a bag, a glass vial, a plastic vial, or a bottle.

[0041] In embodiments, liquid pharmaceutical compositions for parenteral administration to a subject including gaboxadol or a pharmaceutically acceptable salt thereof at a concentration of about 0.005 μg/ml to about 500 μg/ml are provided. In embodiments, the composition includes gaboxadol or a pharmaceutically acceptable salt thereof at a concentration of, *e.g.*, about 0.005 μg/ml to about 250 μg/ml, about 0.005 μg/ml to about 200 μg/ml, about 0.005 μg/ml to about 150 μg/ml, about 0.005 μg/ml to about 100 μg/ml, or about 0.005 μg/ml to about 50 μg/ml.

[0042] In embodiments, compositions for parenteral administration include gaboxadol or a pharmaceutically acceptable salt thereof at a concentration of, *e.g.*, about 0.05 μg/ml to about 50 μg/ml, about 0.1 μg/ml to about 50 μg/ml, about 0.05 μg/ml to about 25 μg/ml, about 0.05 μg/ml to about 10 μg/ml, about 0.05 μg/ml to about 5 μg/ml, or about 0.05 μg/ml to about 1 μg/ml. In embodiments, a composition for parenteral administration includes gaboxadol or a pharmaceutically acceptable salt thereof at a concentration of, *e.g.*, about 0.05 μg/ml to about 15 μg/ml, about 0.5 μg/ml to about 10 μg/ml, about 0.5 μg/ml to about 7 μg/ml, about 1 μg/ml to about 10 μg/ml, about 5 μg/ml to about 10 μg/ml, or about 5 μg/ml to about 15 μg/ml. In embodiments, pharmaceutical compositions for parenteral administration are formulated as a total volume of about, *e.g.*, 10 ml, 20 ml, 25 ml, 50 ml, 100 ml, 200 ml, 250 ml, or 500 ml.

[0043] In embodiments, compositions for parenteral administration including about 0.05 mg to about 100 mg gaboxadol or a pharmaceutically acceptable salt thereof are provided. In embodiments, the pharmaceutical compositions include about, *e.g.*, 0.1 mg to 25 mg, 0.1 mg to 20 mg, 0.1 mg to 15 mg, 0.5 mg to 25 mg, 0.5 mg to 20 mg, 0.5 to 15 mg, 1 mg to 25 mg, 1 mg to 20 mg, 1 mg to 15 mg, 1.5 mg to 25 mg, 1.5 mg to 20 mg, 1.5 mg to 15 mg, 2 mg to 25 mg, 2 mg to 20 mg, 2 mg to 15 mg, 2.5 mg to 25 mg, 2.5 mg to 20 mg, 2.5 mg to 15 mg, 3 mg to 25 mg, 3 mg to 20 mg, 3 mg to 15 mg gaboxadol or a pharmaceutically acceptable salt thereof.

[0044] In embodiments, the pharmaceutical compositions for parenteral administration include about, *e.g.*, 5 mg to 20 mg, 5 mg to 10 mg, 4 mg to 6 mg, 6 mg to 8 mg, 8 mg to 10 mg, 10 mg to 12 mg, 12 mg to 14 mg, 14 mg to 16 mg, 16 mg to 18 mg, or 18 mg to 20 mg gaboxadol or a pharmaceutically acceptable salt thereof. In embodiments, the pharmaceutical compositions for parenteral administration include about, *e.g.*, 0.1 mg, 0.25 mg, 0.5 mg, 1 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 7 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg, 17.5 mg, 20 mg gaboxadol or a pharmaceutically acceptable salt thereof or amounts that are multiples of such doses.

[0045] In embodiments, pharmaceutical compositions for parenteral administration including gaboxadol or a pharmaceutically acceptable salt thereof wherein the gaboxadol or pharmaceutically acceptable salt thereof is present at a molarity less than about 1.0 M are provided. In embodiments, gaboxadol or pharmaceutically acceptable salt thereof is present at a molarity greater than, *e.g.*, about 0.0001 M about 0.001 M, about 0.01 M, about 0.1 M, about 0.2 M, greater than about 0.5, greater than about 1.0 M, greater than about 1.2 M, greater than about 1.5 M, greater than about 1.75 M, greater than about 2.0 M, or greater than

about 2.5 M. In embodiments, gaboxadol or pharmaceutically acceptable salt thereof is present at a molarity of between, *e.g.*, about 0.00001 M to about 0.1 M, about 0.01 to about 0.1 M, about 0.1 M to about 1.0 M, about 1.0 M to about 5.0 M, or about 5.0 M to about 10.0 M. In embodiments, gaboxadol or pharmaceutically acceptable salt thereof is present at a molarity of less than, *e.g.*, about 0.01 M, about 0.1 M, about 1.0 M, about 5.0 M, or about 10.0 M

[0046] In embodiments, the solubility of gaboxadol or pharmaceutically acceptable salt thereof in the composition for parenteral administration is greater than, *e.g.*, about 10 mg/mL, about 15 mg/mL, about 20 mg/mL, about 25 mg/mL, about 30 mg/mL, about 40 mg/mL, about 50 mg/mL, about 75 mg/mL, about 100 mg/mL, about 150 mg/mL, when measured, for example, in water at 25°C.

[0047] In embodiments, the solubility of gaboxadol or pharmaceutically acceptable salt thereof in the composition for parenteral administration is between, *e.g.*, about 1 mg/mL to about 50 mg/mL, about 5 mg/mL to about 50 mg/mL, about 10 mg/mL to about 50 mg/mL, about 20 mg/mL to about 50 mg/ml, from about 20 mg/mL to about 30 mg/mL or from about 10 mg/mL to about 45 mg/mL, when measured, for example, in water at 25 C.

[0048] In embodiments, a pharmaceutical composition for parenteral administration is provided wherein the pharmaceutical composition is stable for at least six months. In embodiments, the pharmaceutical compositions herein exhibit no more than about 5% decrease in gaboxadol or pharmaceutically acceptable salt thereof after, *e.g.*, 3 months or 6 months. In embodiments, the amount of gaboxadol or pharmaceutically acceptable salt thereof degradation is no more than about, *e.g.*, 2.5%, 1%, 0.5% or 0.1%. In embodiments, the degradation of gaboxadol or pharmaceutically acceptable salt thereof is less than about, *e.g.*, 5%, 2.5%, 1%, 0.5%, 0.25%, 0.1%, for at least six months.

[0049] In embodiments, pharmaceutical compositions for parenteral administration wherein the pharmaceutical composition remains soluble are provided. In embodiments, pharmaceutical compositions that are stable, soluble, local site compatible and/or ready-to-use are provided. In embodiments, the pharmaceutical compositions herein are ready-to-use for direct administration to a patient in need thereof.

[0050] The parenteral compositions herein may include one or more excipients, *e.g.*, solvents, solubility enhancers, suspending agents, buffering agents, isotonicity agents, stabilizers or antimicrobial preservatives. When used, the excipients of the parenteral compositions will not adversely affect the stability, bioavailability, safety, and/or efficacy of gaboxadol or pharmaceutically acceptable salt used in the composition. Thus, parenteral

compositions are provided wherein there is no incompatibility between any of the components of the dosage form.

[0051] Thus, in embodiments, parenteral compositions of gaboxadol or a pharmaceutically acceptable salt thereof including a stabilizing amount of at least one excipient are provided. For example, excipients may be selected buffering agents, solubilizing agents, tonicity agents, antioxidants, chelating agents, antimicrobial agents, preservatives, and combinations thereof. One skilled in the art will appreciate that an excipient may have more than one function and be classified in one or more defined group.

[0052] In embodiments, pharmaceutical compositions for parenteral administration are provided including gaboxadol, or a pharmaceutically acceptable salt thereof and an excipient wherein the excipient comprises a stabilizing amount of a buffering agent. In embodiments, the buffering agent can be a citrate, phosphate, acetate, tartrate, carbonate, glutamate, lactate, succinate, bicarbonate buffer and combinations thereof. For example, sodium citrate, trisodium citrate anhydrous, trisodium citrate dihydrate, sodium citrate dehydrate, triethanolamine (TRIS), trisodium citrate pentahydrate dihydrate (*i.e.*, trisodium citrate dehydrate), acetic acid, citric acid, glutamic acid, phosphoric acid, may be used as a buffering agent. In embodiments, the buffering agent may be an amino acid, alkali metal, or alkaline earth metal buffer. For example, the buffering agent may be sodium acetate or hydrogen phosphate. In embodiments, provided herein are parenteral compositions of gaboxadol of pharmaceutically acceptable salts thereof wherein the pH of the composition is between about 4.0 to about 8.0. In embodiments, the pH of the compositions is between, *e.g.*, about 5.0 to about 8.0, about 6.0 to about 8.0, about 6.5 to about 8.0. In embodiments, the pH of the compositions is between, *e.g.*, about 6.5 to about 7.5, about 7.0 to about 7.8, about 7.2 to about 7.8, or about 7.3 to about 7.6. In embodiments, the pH of the aqueous solution of gaboxadol is, *e.g.*, about 6.8, about 7.0, about 7.2, about 7.4, about 7.6, about 7.7, about 7.8, about 8.0, about 8.2, about 8.4, or about 8.6.

[0053] In embodiments, pharmaceutical compositions for parenteral administration are provided including gaboxadol, or a pharmaceutically acceptable salt thereof and an excipient wherein the excipient includes a solubilizing agent. For example, solubilizing agents according to the invention may include, *e.g.*, sodium hydroxide, L-lysine, L-arginine, sodium carbonate, potassium carbonate, sodium phosphate, and/or potassium phosphate. In embodiments, provided herein are pharmaceutical compositions including gaboxadol, or a pharmaceutically acceptable salt thereof and an excipient wherein the excipient includes a particulate formation inhibitor. A particulate formation inhibitor refers to a compound that

has the desired property of inhibiting the formation of particles in parenteral compositions. Particulate formation inhibitors of the invention include ethylenediaminetetraacetic acid (EDTA) and salts thereof, for example, ethylenediaminetetraacetic acid, calcium disodium salt (preferably as the hydrate); ethylenediaminetetraacetic acid, diammonium salt (preferably as the hydrate); ethylenediaminetetraacetic acid, dipotassium salt (preferably as the dihydrate); ethylenediaminetetraacetic acid, disodium salt (preferably as the dihydrate and, if desired, as the anhydrous form); ethylenediaminetetraacetic acid, tetrasodium salt (preferably as the hydrate); ethylenediaminetetraacetic acid, tripotassium salt (preferably as the dihydrate); ethylenediaminetetraacetic acid, trisodium salt (preferably as the hydrate) and ethylenediaminetetraacetic acid disodium salt, USP(preferably as the dihydrate).

[0054] In embodiments, provided herein are pharmaceutical compositions for parenteral administration including gaboxadol, or a pharmaceutically acceptable salt thereof and an excipient wherein the excipient includes a solubilizing agent. For example, solubilizing agents may include, but are not limited to, acids, such as carboxylic acids, amino acids. In other examples, the solubilizing agents may be saturated carboxylic acids, unsaturated carboxylic acids, fatty acids, keto acids, aromatic carboxylic acids, dicarboxylic acids, tricarboxylic acids, α-hydroxy acids, amino acids, formic acid, acetic acid, propionic acid, butyric acid, valeric acid, caproic acid, enanthic acid, caprylic acid, pelargonic acid, capric acid, lauric acid, stearic acid, acrylic acid, docosahexaenoic acid, eicosapentaenoic acid, pyruvic acid, benzoic acid, salicylic acid, aldaric acid, oxalic acid, malonic acid, malic acid, succinic acid, glutaric acid, adipic acid, citric acid, lactic acid, alanine, arginine, aspargine, aspartic acid, cysteine, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, praline, serine, threonine, tryptophan, tyrosine, valine, and combinations thereof.

[0055] In embodiments, provided herein are pharmaceutical compositions for parenteral administration including gaboxadol or a pharmaceutically acceptable salt thereof and an excipient wherein the excipient renders the composition isotonic. Isotonic pharmaceutical compositions herein may be achieved by adding an appropriate quantity of sodium chloride, glucose, laevulose, dextrose, mannitol, or postassium chloride, or calcium chloride, or calcium gluconoglucoheptonate, or mixtures thereof. In embodiments, provided herein are pharmaceutical compositions including gaboxadol, or a pharmaceutically acceptable salt thereof and an excipient wherein the excipient includes a free radical antagonist. In embodiments, the free radical antagonist is ascorbic acid, ascorbic acid derivatives, organic

compounds having at least one thiol, alkyl polyhydroxylated, and cycloalkyl polyhydroxylated compounds, and combinations thereof.

[0056] In embodiments, provided herein are pharmaceutical compositions for parenteral administration including gaboxadol, or a pharmaceutically acceptable salt thereof and an excipient wherein the excipient includes a preservative. In embodiments, the preservative is selected from benzalkonium chloride, benzethonium chloride, benzyl alcohol, chlorobutanol, chlorocresol, metacresol, Phenol, phenylmercuric nitrate, phenylmercuric acetate, methyl p-hydroxybenzoate, propyl p-hydroxybenzoate, butyl p-hydroxybenzoate, and thimerosal. In other embodiments, the preservative is selected from the group consisting of phenol, meta-cresol, benzyl alcohol, parabens (*e.g.*, methyl, propyl, butyl), benzalkonium chloride, chlorobutanol, thimerosal, phenylmercuric salts (*e.g.*, acetate, borate, or nitrate), and combinations thereof.

[0057] When administered, the parenteral compositions herein provide a time of maximum plasma concentration (T_{max}) for gaboxadol in human patients of about 1 or more hours (*e.g.*, about 1.5 or more hours). In embodiments, a T_{max} of gaboxadol in human patients ranging from between, *e.g.*, about 1 to about 5 hours, about 1 to about 4 hours, about 1 to about 3 hours, about 1 to about 2 hours. In embodiments, a T_{max} for gaboxadol in human patients of more than about 1.5 is observed. In embodiments, a T_{max} for gaboxadol in human patients of less than about 3 hours is observed. The time of maximum plasma concentration is measured once infusion is complete.

[0058] In embodiments herein a dosage form includes from about 1 mg to about 500 mg gaboxadol, wherein parenteral administration (*e.g.*, intramuscular, intravenous, subcutaneous, intraperitoneal, or intrathecal) of the dosage form provides an *in vivo* plasma profile for gaboxadol comprising a mean $AUC_{0-\infty}$ of more than about 25 ng•hr/ml. In embodiments, single dose administration of the dosage form provides an *in vivo* plasma profile for gaboxadol comprising a mean $AUC_{0-\infty}$ of more than about, *e.g.*, 50 ng•hr/ml, 75 ng•hr/ml, 150 ng•hr/ml, 250 ng•hr/ml, 500 ng•hr/ml, 1000 ng•hr/ml, or 1500 ng•hr/ml.

[0059] In embodiments, the dosage form for parenteral administration includes from about 1 mg to about 500 mg gaboxadol, wherein administration of the dosage form provides an *in vivo* plasma profile for gaboxadol comprising a mean C_{max} of less than about 10000 ng/ml. In embodiments, single dose administration of the compositions for parenteral administration provide an *in vivo* plasma profile for gaboxadol of a mean C_{max} of less than about, *e.g.*, 5000 ng/ml, 2500 ng/ml, 1000 ng/ml, 500 ng/ml, 250 ng/ml, or 100 ng/ml.

[0060] In embodiments, pharmaceutical compositions for parenteral administration include gaboxadol or a pharmaceutically acceptable salt thereof wherein parenteral administration exhibits a pharmacokinetic profile of a T_{max} at about 1 to about 120 minutes after administration of the parenteral composition; followed by a plasma drug concentration of at least 50% C_{max} for a duration of about 90 to about 360 minutes. In embodiments, parenteral administration of gaboxadol is followed by a plasma drug concentration of at least 50% C_{max} for a duration of, *e.g.*, about 10 to about 60 minutes, about 15 to about 90 minutes, about 30 to about 120 minutes, about 60 to about 180 minutes, about 90 to about 180 minutes.

[0061] Pharmaceutical compositions herein may be provided with immediate release, delayed release, extended release, or modified release profiles. In embodiments, pharmaceutical compositions with different drug release profiles may be combined to create a two phase or three-phase release profile. For example, pharmaceutical compositions may be provided with an immediate release and an extended release profile. In embodiments, pharmaceutical compositions may be provided with an extended release and delayed release profile. Such composition may be provided as pulsatile formulations, multilayer tablets, or capsules containing tablets, beads, granules, etc. Compositions may be prepared using a pharmaceutically acceptable "carrier" composed of materials that are considered safe and effective. The "carrier" includes all components present in the pharmaceutical formulation other than the active ingredient or ingredients. The term "carrier" includes, but is not limited to, diluents, binders, lubricants, disintegrants, fillers, and coating compositions.

[0062] In embodiments, the pharmaceutical compositions described herein may be administered once, twice, or three times daily, or every other day. In embodiments, a pharmaceutical composition described herein is provided to the patient in the evening. In embodiments, a pharmaceutical composition described herein is provided to the patient at bedtime. In embodiments, a pharmaceutical composition described herein is provided to the patient once in the evening and once in the morning. In embodiments, the total amount of gaboxadol or a pharmaceutically acceptable salt thereof administered to a subject in a 24-hour period is 1 mg to 30 mg. In embodiments, the total amount of gaboxadol or a pharmaceutically acceptable salt thereof administered to a subject in a 24-hour period is 1 mg to 20 mg. In embodiments, the total amount of gaboxadol or a pharmaceutically acceptable salt thereof administered to a subject in a 24-hour period is 5 mg, 10 mg, or 15 mg. In embodiments, the total amount of gaboxadol or a pharmaceutically acceptable salt thereof administered to a subject in a 24-hour period is 20 mg.

[0063] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement in at least one symptom of the IBS. Symptoms of IBS may include, but are not limited to, cramping, repeated abdominal pain, bloating, and changes in bowel movements which may be diarrhea, constipation, or both.

[0064] In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement in at least one symptom of the Crohn's disease. Symptoms of Crohn's disease may include, but are not limited to, diarrhea, cramping, abdominal pain, anemia, fever and nausea.

[0065] In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement in at least one symptom of the celiac disease. Symptoms of celiac disease may include, but are not limited to, bloating, chronic diarrhea, constipation, gas, nausea, pale, foul smelling stools, stomach pain and malabsorption of nutrients, delayed puberty, failure to thrive in infants, slowed growth and weight loss.

[0066] In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement in at least one symptom of the ulcerative colitis. Symptoms of the ulcerative colitis may include, but are not limited to, urgent need to have a bowel movement, bloody bowel movements, fevers, severe abdominal cramping, fatigue, nausea, loss of appetite, weight loss, fever, anemia, joint pain, and rashes.

[0067] In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement in at least one symptom of the microscopic colitis. Symptoms of microscopic colitis may include, but are not limited to, chronic, watery, non-bloody diarrhea, a strong urgency to have a bowel movement, pain, cramping, bloating, weight loss, nausea, and fecal incontinence.

[0068] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol

or a pharmaceutically acceptable salt thereof wherein the composition provides improvement in at least one symptom of the asthma. Symptoms of asthma may include, but are not limited to, wheezing, chest tightness, shortness of breath, and coughing.

[0069] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement of at least one IBS symptom for more than 4 hours after administration of the pharmaceutical composition to the patient. In embodiments, the improvement of at least one IBS symptom for more than 6 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement of at least one IBS symptom for more than, e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement in at least one IBS symptom for at least e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement in at least one IBS symptom for 12 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure.

[0070] In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement of at least one Crohn's disease symptom for more than 4 hours after administration of the pharmaceutical composition to the patient. In embodiments, the improvement of at least one Crohn's disease symptom for more than 6 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement of at least one Crohn's disease symptom for more than, e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement in at least one Crohn's disease symptom for at least e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement in at least one Crohn's disease symptom for 12 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure.

[0071] In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement of at least one celiac disease symptom for more than 4 hours after administration of the pharmaceutical composition to the patient. In embodiments, the improvement of at least one celiac disease symptom for more than 6 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement of at least one celiac disease symptom for more than, e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement in at least one celiac disease symptom for at least e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement in at least one celiac disease symptom for 12 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure.

[0072] In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement of at least one ulcerative colitis symptom for more than 4 hours after administration of the pharmaceutical composition to the patient. In embodiments, the improvement of at least one ulcerative colitis symptom for more than 6 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement of at least one ulcerative colitis symptom for more than, e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement in at least one ulcerative colitis symptom for at least e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement in at least one ulcerative colitis symptom for 12 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure.

[0073] In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including

gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement of at least one microscopic colitis symptom for more than 4 hours after administration of the pharmaceutical composition to the patient. In embodiments, the improvement of at least one microscopic colitis symptom for more than 6 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement of at least one microscopic colitis symptom for more than, e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement in at least one microscopic colitis symptom for at least e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement in at least one microscopic colitis symptom for 12 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure.

[0074] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement of at least one asthma symptom for more than 4 hours after administration of the pharmaceutical composition to the patient. In embodiments, the improvement of at least one asthma symptom for more than 6 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement of at least one asthma symptom for more than, e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement in at least one asthma symptom for at least e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure. In embodiments, improvement in at least one asthma symptom for 12 hours after administration of the pharmaceutical composition to the patient is provided in accordance with the present disclosure.

[0075] FIG. 1 shows the arithmetic mean plasma concentration-time profiles of gaboxadol following single oral doses (2.5, 5, 10, 15, and 20 mg)(see, Example 1, below) with horizontal lines Δ indicating the change between 6 and 12 hours. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof about

0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 50% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 55% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 60% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 65% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 70% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by

more than 75% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0076] In embodiments, provided herein are methods of treating IBS wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is less than about 75% of the administered dose. In embodiments, provided herein are methods wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is less than about 75%.

[0077] In embodiments, provided herein are methods of treating IBS wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is less than about 80% of the administered dose. In embodiments, provided herein are methods wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is less than about 80% of the administered dose.

[0078] In embodiments, provided herein are methods of treating IBS wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is between about 65% to about 85% of the administered dose. In embodiments, the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient after about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is between about 65% to about 85% of the administered dose.

[0079] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 75% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 80% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of

treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 85% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 90% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 95% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 100% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0080] In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 50% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 55% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating

Crohn's disease including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 60% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 65% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 70% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 75% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0081] In embodiments, provided herein are methods of treating Crohn's disease wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is less than about 75% of the administered dose. In embodiments, provided herein are methods wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is less than about 75%.

[0082] In embodiments, provided herein are methods of treating Crohn's disease wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is less than about 80% of the

administered dose. In embodiments, provided herein are methods wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is less than about 80% of the administered dose.

[0083] In embodiments, provided herein are methods of treating Crohn's disease wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is between about 65% to about 85% of the administered dose. In embodiments, the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient after about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is between about 65% to about 85% of the administered dose.

[0084] In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 75% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 80% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 85% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 90% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical

composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 95% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 100% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0085] In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 50% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 55% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 60% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 65% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours

after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 70% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 75% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0086] In embodiments, provided herein are methods of treating celiac disease wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is less than about 75% of the administered dose. In embodiments, provided herein are methods wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is less than about 75%.

[0087] In embodiments, provided herein are methods of treating celiac disease wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is less than about 80% of the administered dose. In embodiments, provided herein are methods wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is less than about 80% of the administered dose.

[0088] In embodiments, provided herein are methods of treating celiac disease wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is between about 65% to about 85% of the administered dose. In embodiments, the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient after about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is between about 65% to about 85% of the administered dose.

[0089] In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 75% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 80% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 85% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 90% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 95% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 100% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0090] In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a

pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 50% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 55% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 60% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 65% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 70% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 75%

and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0091] In embodiments, provided herein are methods of treating ulcerative colitis wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is less than about 75% of the administered dose. In embodiments, provided herein are methods wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is less than about 75%.

[0092] In embodiments, provided herein are methods of treating ulcerative colitis wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is less than about 80% of the administered dose. In embodiments, provided herein are methods wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is less than about 80% of the administered dose.

[0093] In embodiments, provided herein are methods of treating ulcerative colitis wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is between about 65% to about 85% of the administered dose. In embodiments, the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient after about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is between about 65% to about 85% of the administered dose.

[0094] In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 75% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 80% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments,

provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 85% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 90% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 95% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 100% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0095] In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 50% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 55% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or

24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 60% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 65% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 70% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 75% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0096] In embodiments, provided herein are methods of treating microscopic colitis wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is less than about 75% of the administered dose. In embodiments, provided herein are methods wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is less than about 75%.

[0097] In embodiments, provided herein are methods of treating microscopic colitis wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about

4 hours after administration of the pharmaceutical composition is less than about 80% of the administered dose. In embodiments, provided herein are methods wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is less than about 80% of the administered dose.

[0098] In embodiments, provided herein are methods of treating microscopic colitis wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is between about 65% to about 85% of the administered dose. In embodiments, the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient after about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is between about 65% to about 85% of the administered dose.

[0099] In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 75% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 80% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 85% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 90% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments,

provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 95% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 100% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0100] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 50% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 55% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 60% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 65% and the method

provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 70% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 75% and the method provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0101] In embodiments, provided herein are methods of treating asthma wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is less than about 75% of the administered dose. In embodiments, provided herein are methods wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is less than about 75%.

[0102] In embodiments, provided herein are methods of treating asthma wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is less than about 80% of the administered dose. In embodiments, provided herein are methods wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about, *e.g.*, 6 hours, 8 hours, 10 hours, 12 hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is less than about 80% of the administered dose.

[0103] In embodiments, provided herein are methods of treating asthma wherein the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient about 4 hours after administration of the pharmaceutical composition is between about 65% to about 85% of the administered dose. In embodiments, the amount of gaboxadol or pharmaceutically acceptable salt thereof within the patient after about, *e.g.*, 6 hours, 8 hours, 10 hours, 12

hours, 15 hours, or 20 hours after administration of the pharmaceutical composition is between about 65% to about 85% of the administered dose.

[0104] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 75% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 80% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 85% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 90% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 95% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma concentration 6 hours after administration which is less than 100% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0105] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a C_{max} less than about 500 ng/ml. In embodiments, the composition provides improvement for more than 6 hours after administration to the patient.

[0106] In embodiments, the composition provides an *in vivo* plasma profile having a C_{max} less than about, *e.g.*, 450 ng/ml, 400 ng/ml 350 ng/ml, or 300 ng/ml and wherein the composition provides improvement in one or more symptoms of IBS a day after administration. In embodiments, the composition provides an *in vivo* plasma profile having a C_{max} less than about, *e.g.*, 250 ng/ml, 200 ng/ml 150 ng/ml, or 100 ng/ml and wherein the composition provides improvement in one or more symptoms of IBS a day after administration.

[0107] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about 900 ng•hr/ml. In embodiments, the composition provides improvement in one or more symptoms of IBS a day after administration. In embodiments, the compositions provide an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 850 ng•hr/ml, 800 ng•hr/ml, 750 ng•hr/ml, or 700 ng•hr/ml and wherein the composition provides improvement in one or more symptoms of IBS a day after administration. In embodiments, the composition provides improvement in one or more IBS symptoms for more than 6 hours after administration.

[0108] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 650 ng•hr/ml, 600 ng•hr/ml, 550 ng•hr/ml, 500 ng•hr/ml, or 450 ng•hr/ml . In embodiments, wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 400 ng•hr/ml, 350 ng•hr/ml, 300 ng•hr/ml, 250 ng•hr/ml, or 200 ng•hr/ml. In embodiments, the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 150 ng•hr/ml, 100 ng•hr/ml, 75 ng•hr/ml, or 50 ng•hr/ml. In embodiments, the composition provides improvement symptoms of IBS for more than, *e.g.*, 4 hours, 6 hours, 8 hours, 10 hours, or 12 hours, after administration of the composition to the patient.

[0109] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0110] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a

pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0111] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including

administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0112] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile having a mean $AUC_{0-\infty}$ of at least about 20% less than the first pharmaceutical composition.

[0113] In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a C_{max} less than about 500 ng/ml. In embodiments, the composition provides improvement for more than 6 hours after administration to the patient.

[0114] In embodiments, the composition provides an *in vivo* plasma profile having a C_{max} less than about, *e.g.*, 450 ng/ml, 400 ng/ml 350 ng/ml, or 300 ng/ml and wherein the composition provides improvement in one or more symptoms of Crohn's disease a day after

administration. In embodiments, the composition provides an *in vivo* plasma profile having a C_{max} less than about, *e.g.*, 250 ng/ml, 200 ng/ml 150 ng/ml, or 100 ng/ml and wherein the composition provides improvement in one or more symptoms of Crohn's disease a day after administration.

[0115] In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about 900 ng•hr/ml. In embodiments, the composition provides improvement in one or more symptoms of Crohn's disease a day after administration. In embodiments, the compositions provide an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 850 ng•hr/ml, 800 ng•hr/ml, 750 ng•hr/ml, or 700 ng•hr/ml and wherein the composition provides improvement in one or more symptoms of Crohn's disease a day after administration. In embodiments, the composition provides improvement in one or more Crohn's disease symptoms for more than 6 hours after administration.

[0116] In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 650 ng•hr/ml, 600 ng•hr/ml, 550 ng•hr/ml, 500 ng•hr/ml, or 450 ng•hr/ml . In embodiments, wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 400 ng•hr/ml, 350 ng•hr/ml, 300 ng•hr/ml, 250 ng•hr/ml, or 200 ng•hr/ml. In embodiments, the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 150 ng•hr/ml, 100 ng•hr/ml, 75 ng•hr/ml, or 50 ng•hr/ml. In embodiments, the composition provides improvement symptoms of Crohn's disease for more than, *e.g.*, 4 hours, 6 hours, 8 hours, 10 hours, or 12 hours, after administration of the composition to the patient.

[0117] In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the C_{max} and provides

improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0118] In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the C_{max} and provides

improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0119] In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a

pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0120] In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile having a mean $AUC_{0-\infty}$ of at least about 20% less than the first pharmaceutical composition.

[0121] In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a C_{max} less than about 500 ng/ml. In embodiments, the composition provides improvement for more than 6 hours after administration to the patient.

[0122] In embodiments, the composition provides an *in vivo* plasma profile having a C_{max} less than about, *e.g.*, 450 ng/ml, 400 ng/ml 350 ng/ml, or 300 ng/ml and wherein the composition provides improvement in one or more symptoms of celiac disease a day after administration. In embodiments, the composition provides an *in vivo* plasma profile having a C_{max} less than about, *e.g.*, 250 ng/ml, 200 ng/ml 150 ng/ml, or 100 ng/ml and wherein the composition provides improvement in one or more symptoms of celiac disease a day after administration.

[0123] In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about 900 ng•hr/ml. In embodiments, the composition provides improvement in one or more symptoms of celiac disease a day after administration. In embodiments, the compositions provide an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 850 ng•hr/ml, 800 ng•hr/ml, 750 ng•hr/ml, or 700 ng•hr/ml and wherein the composition provides improvement in one or more symptoms of celiac disease a day after administration. In embodiments, the composition provides improvement in one or more celiac disease symptoms for more than 6 hours after administration.

[0124] In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 650 ng•hr/ml, 600 ng•hr/ml, 550 ng•hr/ml, 500 ng•hr/ml, or 450 ng•hr/ml . In embodiments, wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 400 ng•hr/ml, 350 ng•hr/ml, 300 ng•hr/ml, 250 ng•hr/ml, or 200 ng•hr/ml. In embodiments, the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 150 ng•hr/ml, 100 ng•hr/ml, 75 ng•hr/ml, or 50 ng•hr/ml. In embodiments, the composition provides improvement symptoms of celiac disease for more than, *e.g.*, 4 hours, 6 hours, 8 hours, 10 hours, or 12 hours, after administration of the composition to the patient.

[0125] In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a

AUC_{6-12} which is less than 85% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0126] In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an

in vivo plasma profile having a AUC_{6-12} which is less than 90% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0127] In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease

including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0128] In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile having a mean $AUC_{0-\infty}$ of at least about 20% less than the first pharmaceutical composition.

[0129] In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a C_{max} less than about 500 ng/ml. In embodiments, the composition provides improvement for more than 6 hours after administration to the patient.

[0130] In embodiments, the composition provides an *in vivo* plasma profile having a C_{max} less than about, *e.g.*, 450 ng/ml, 400 ng/ml 350 ng/ml, or 300 ng/ml and wherein the composition provides improvement in one or more symptoms of ulcerative colitis a day after administration. In embodiments, the composition provides an *in vivo* plasma profile having a C_{max} less than about, *e.g.*, 250 ng/ml, 200 ng/ml 150 ng/ml, or 100 ng/ml and wherein the composition provides improvement in one or more symptoms of ulcerative colitis a day after administration.

[0131] In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about 900 ng•hr/ml. In embodiments, the composition provides improvement in one or more symptoms of ulcerative colitis a day after

administration. In embodiments, the compositions provide an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 850 ng•hr/ml, 800 ng•hr/ml, 750 ng•hr/ml, or 700 ng•hr/ml and wherein the composition provides improvement in one or more symptoms of ulcerative colitis a day after administration. In embodiments, the composition provides improvement in one or more ulcerative colitis symptoms for more than 6 hours after administration.

[0132] In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 650 ng•hr/ml, 600 ng•hr/ml, 550 ng•hr/ml, 500 ng•hr/ml, or 450 ng•hr/ml . In embodiments, wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 400 ng•hr/ml, 350 ng•hr/ml, 300 ng•hr/ml, 250 ng•hr/ml, or 200 ng•hr/ml. In embodiments, the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 150 ng•hr/ml, 100 ng•hr/ml, 75 ng•hr/ml, or 50 ng•hr/ml. In embodiments, the composition provides improvement symptoms of ulcerative colitis for more than, *e.g.*, 4 hours, 6 hours, 8 hours, 10 hours, or 12 hours, after administration of the composition to the patient.

[0133] In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the C_{max} and

provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a $AUC_{6\text{-}12}$ which is less than 95% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a $AUC_{6\text{-}12}$ which is less than 100% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0134] In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{6\text{-}12}$ which is less than 75% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{6\text{-}12}$ which is less than 80% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{6\text{-}12}$ which is less than 85% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{6\text{-}12}$ which is less than 90% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an

in vivo plasma profile having a AUC_{6-12} which is less than 95% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0135] In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours

after administration. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0136] In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile having a mean $AUC_{0-\infty}$ of at least about 20% less than the first pharmaceutical composition.

[0137] In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a C_{max} less than about 500 ng/ml. In embodiments, the composition provides improvement for more than 6 hours after administration to the patient.

[0138] In embodiments, the composition provides an *in vivo* plasma profile having a C_{max} less than about, *e.g.*, 450 ng/ml, 400 ng/ml 350 ng/ml, or 300 ng/ml and wherein the composition provides improvement in one or more symptoms of microscopic colitis a day after administration. In embodiments, the composition provides an *in vivo* plasma profile having a C_{max} less than about, *e.g.*, 250 ng/ml, 200 ng/ml 150 ng/ml, or 100 ng/ml and wherein the composition provides improvement in one or more symptoms of microscopic colitis a day after administration.

[0139] In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about 900 ng•hr/ml. In embodiments, the composition provides improvement in one or more symptoms of microscopic colitis a day after administration. In embodiments, the compositions provide an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 850 ng•hr/ml, 800 ng•hr/ml, 750 ng•hr/ml, or 700 ng•hr/ml and wherein the composition provides improvement in one or more symptoms of microscopic colitis a day after administration. In embodiments, the composition provides

improvement in one or more microscopic colitis symptoms for more than 6 hours after administration.

[0140] In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 650 ng•hr/ml, 600 ng•hr/ml, 550 ng•hr/ml, 500 ng•hr/ml, or 450 ng•hr/ml . In embodiments, wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 400 ng•hr/ml, 350 ng•hr/ml, 300 ng•hr/ml, 250 ng•hr/ml, or 200 ng•hr/ml. In embodiments, the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 150 ng•hr/ml, 100 ng•hr/ml, 75 ng•hr/ml, or 50 ng•hr/ml. In embodiments, the composition provides improvement symptoms of microscopic colitis for more than, *e.g.*, 4 hours, 6 hours, 8 hours, 10 hours, or 12 hours, after administration of the composition to the patient.

[0141] In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof an

amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0142] In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis

including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0143] In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition

provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0144] In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile having a mean $AUC_{0-\infty}$ of at least about 20% less than the first pharmaceutical composition.

[0145] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a C_{max} less than about 500 ng/ml. In embodiments, the composition provides improvement for more than 6 hours after administration to the patient.

[0146] In embodiments, the composition provides an *in vivo* plasma profile having a C_{max} less than about, *e.g.*, 450 ng/ml, 400 ng/ml 350 ng/ml, or 300 ng/ml and wherein the composition provides improvement in one or more symptoms of asthma a day after administration. In embodiments, the composition provides an *in vivo* plasma profile having a C_{max} less than about, *e.g.*, 250 ng/ml, 200 ng/ml 150 ng/ml, or 100 ng/ml and wherein the composition provides improvement in one or more symptoms of asthma a day after administration.

[0147] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about 900 ng•hr/ml. In embodiments, the composition provides improvement in one or more symptoms of asthma a day after administration. In embodiments, the compositions provide an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 850 ng•hr/ml, 800 ng•hr/ml, 750 ng•hr/ml, or 700 ng•hr/ml and wherein the composition provides improvement in one or more symptoms of asthma a day after administration. In embodiments, the composition provides improvement in one or more asthma symptoms for more than 6 hours after administration.

[0148] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol

or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 650 ng•hr/ml, 600 ng•hr/ml, 550 ng•hr/ml, 500 ng•hr/ml, or 450 ng•hr/ml . In embodiments, wherein the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 400 ng•hr/ml, 350 ng•hr/ml, 300 ng•hr/ml, 250 ng•hr/ml, or 200 ng•hr/ml. In embodiments, the composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 150 ng•hr/ml, 100 ng•hr/ml, 75 ng•hr/ml, or 50 ng•hr/ml. In embodiments, the composition provides improvement symptoms of asthma for more than, *e.g.*, 4 hours, 6 hours, 8 hours, 10 hours, or 12 hours, after administration of the composition to the patient.

[0149] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof an amount of gaboxadol or a pharmaceutically

acceptable salt thereof which provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0150] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the C_{max} and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0151] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 75% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 80% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 85% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 90% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 95% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides an *in vivo* plasma profile having a AUC_{6-12} which is less than 100% of the administered dose and provides improvement in the patient for more than 6, 8, 10, 12, 14, 16, 18, 20, 22 or 24 hours after administration.

[0152] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical

composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile having a mean $AUC_{0-\infty}$ of at least about 20% less than the first pharmaceutical composition.

[0153] In embodiments involving administration of a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof, and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof, the first and/or the second pharmaceutical compositions may be administered once, twice, or three times daily, or every other day. In embodiments, the first or the second pharmaceutical composition is provided to the patient in the evening. In embodiments, the second pharmaceutical composition includes an amount of gaboxadol that is at least one third of the amount of gaboxadol provided in the first pharmaceutical composition. In embodiments, the second pharmaceutical composition includes an amount of gaboxadol that is at least half of the amount of gaboxadol provided in the first pharmaceutical composition.

[0154] In embodiments, the first or the second pharmaceutical composition is provided to the patient once in the evening and once in the morning. In embodiments, the total amount of gaboxadol or pharmaceutically acceptable salt thereof administered to a subject in a 24-hour period is 1 mg to 30 mg. In embodiments, the total amount of gaboxadol or a pharmaceutically acceptable salt thereof administered to a subject in a 24-hour period is 1 mg to 20 mg. In embodiments, the total amount of gaboxadol or a pharmaceutically acceptable salt thereof administered to a subject in a 24-hour period is 10 mg, 15 mg, or 20 mg. In embodiments, the total amount of gaboxadol or a pharmaceutically acceptable salt thereof administered to a subject in a 24-hour period is 20 mg.

[0155] In embodiments, the first and/or the second pharmaceutical compositions may be provided with immediate release, delayed release, extended release, or modified release profiles. The first and second pharmaceutical compositions may be provided at the same time or separated by an interval of time, *e.g.*, 6 hours, 12 hours etc. In embodiments, the first and the second pharmaceutical compositions may be provided with different drug release profiles to create a two-phase release profile. For example, the first pharmaceutical composition may be provided with an immediate release profile and the second pharmaceutical composition may provide an extended release profile. In embodiments, one or both of the first and second pharmaceutical compositions may be provided with an extended release or delayed release profile. Such compositions may be provided as pulsatile formulations, multilayer tablets or capsules containing tablets, beads, granules, etc. In embodiments, the first pharmaceutical composition is an immediate release composition. In embodiments, the second

pharmaceutical composition is an immediate release composition. In embodiments, the first and second pharmaceutical compositions are provided as separate immediate release compositions, *e.g.*, tablets or capsules. In embodiments the first and second pharmaceutical compositions are provided 12 hours apart.

[0156] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile having a mean $AUC_{0-\infty}$ of at least about, *e.g.*, 25%, 30%, 35%, 40%, 45% or 50% less than the first pharmaceutical composition. In embodiments, the composition provides improvement in one or more symptoms of IBS a day after administration. For example, the composition may provide improvement in one or more symptoms for more than about, *e.g.*, 6 hours, 8 hours, 10 hours, or 12 hours after administration of the first and/or second pharmaceutical composition.

[0157] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile having a mean $AUC_{0-\infty}$ of less than about 900 ng•hr/ml. In embodiments, the second pharmaceutical composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 800 ng•hr/ml, 750 ng•hr/ml, 700 ng•hr/ml, 650 ng•hr/ml, or 600 ng•hr/ml. In embodiments, the second pharmaceutical composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 550 ng•hr/ml, 500 ng•hr/ml, 450 ng•hr/ml, 400 ng•hr/ml, or 350 ng•hr/ml. In embodiments, the second pharmaceutical composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 300 ng•hr/ml, 250 ng•hr/ml, 200 ng•hr/ml, 150 ng•hr/ml, or 100 ng•hr/ml. In embodiments, the first and second pharmaceutical composition are administered wherein the compositions provide improvement of next day functioning of the patient. In embodiments, the first pharmaceutical composition provides improvement in one or more symptoms for more than, *e.g.*, 6 hours, 8 hours or 12 hours after administration of the first pharmaceutical composition.

[0158] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a

pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the first composition provides an *in vivo* plasma profile with a C_{max} that is more than about 50% greater than the C_{max} provided by the administration of the second pharmaceutical composition. As used herein the C_{max} provided by the administration of the second pharmaceutical composition may or may not include the plasma profile contribution of the first pharmaceutical composition. In embodiments, the administration of the second pharmaceutical composition does not include the plasma profile contribution of the first pharmaceutical composition. In embodiments, the first composition provides an *in vivo* plasma profile having a C_{max} that is more than about e.g., 60%, 70%, 80%, or 90% greater than the C_{max} provided by the administration of the second pharmaceutical composition.

[0159] In embodiments, provided herein are methods of treating Crohn's disease, celiac disease ulcerative colitis or microscopic colitis including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile having a mean $AUC_{0-\infty}$ of at least about, *e.g.*, 25%, 30%, 35%, 40%, 45% or 50% less than the first pharmaceutical composition. In embodiments, the composition provides improvement in one or more symptoms of Crohn's disease, celiac disease ulcerative colitis or microscopic colitis a day after administration. For example, the composition may provide improvement in one or more symptoms for more than about, *e.g.*, 6 hours, 8 hours, 10 hours, or 12 hours after administration of the first and/or second pharmaceutical composition.

[0160] In embodiments, provided herein are methods of treating Crohn's disease, celiac disease ulcerative colitis or microscopic colitis including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile having a mean $AUC_{0-\infty}$ of less than about 900 ng•hr/ml. In embodiments, the second pharmaceutical composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 800 ng•hr/ml, 750 ng•hr/ml, 700 ng•hr/ml, 650 ng•hr/ml, or 600 ng•hr/ml. In embodiments, the second pharmaceutical composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 550 ng•hr/ml, 500

ng•hr/ml, 450 ng•hr/ml, 400 ng•hr/ml, or 350 ng•hr/ml. In embodiments, the second pharmaceutical composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 300 ng•hr/ml, 250 ng•hr/ml, 200 ng•hr/ml, 150 ng•hr/ml, or 100 ng•hr/ml. In embodiments, the first and second pharmaceutical composition are administered wherein the compositions provide improvement of next day functioning of the patient. In embodiments, the first pharmaceutical composition provides improvement in one or more symptoms for more than, *e.g.*, 6 hours, 8 hours or 12 hours after administration of the first pharmaceutical composition.

[0161] In embodiments, provided herein are methods of treating Crohn's disease, celiac disease ulcerative colitis or microscopic colitis including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the first composition provides an *in vivo* plasma profile with a C_{max} that is more than about 50% greater than the C_{max} provided by the administration of the second pharmaceutical composition. As used herein the C_{max} provided by the administration of the second pharmaceutical composition may or may not include the plasma profile contribution of the first pharmaceutical composition. In embodiments, the administration of the second pharmaceutical composition does not include the plasma profile contribution of the first pharmaceutical composition. In embodiments, the first composition provides an *in vivo* plasma profile having a C_{max} that is more than about e.g., 60%, 70%, 80%, or 90% greater than the C_{max} provided by the administration of the second pharmaceutical composition.

[0162] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile having a mean $AUC_{0-\infty}$ of at least about, *e.g.*, 25%, 30%, 35%, 40%, 45% or 50% less than the first pharmaceutical composition. In embodiments, the composition provides improvement in one or more symptoms of asthma a day after administration. For example, the composition may provide improvement in one or more symptoms for more than about, *e.g.*, 6 hours, 8 hours, 10 hours, or 12 hours after administration of the first and/or second pharmaceutical composition.

[0163] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the second pharmaceutical composition provides an *in vivo* plasma profile having a mean $AUC_{0-\infty}$ of less than about 900 ng•hr/ml. In embodiments, the second pharmaceutical composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 800 ng•hr/ml, 750 ng•hr/ml, 700 ng•hr/ml, 650 ng•hr/ml, or 600 ng•hr/ml. In embodiments, the second pharmaceutical composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 550 ng•hr/ml, 500 ng•hr/ml, 450 ng•hr/ml, 400 ng•hr/ml, or 350 ng•hr/ml. In embodiments, the second pharmaceutical composition provides an *in vivo* plasma profile having a $AUC_{0-\infty}$ of less than about, *e.g.*, 300 ng•hr/ml, 250 ng•hr/ml, 200 ng•hr/ml, 150 ng•hr/ml, or 100 ng•hr/ml. In embodiments, the first and second pharmaceutical composition are administered wherein the compositions provide improvement of next day functioning of the patient. In embodiments, the first pharmaceutical composition provides improvement in one or more symptoms for more than, *e.g.*, 6 hours, 8 hours or 12 hours after administration of the first pharmaceutical composition.

[0164] In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof wherein the first composition provides an *in vivo* plasma profile with a C_{max} that is more than about 50% greater than the C_{max} provided by the administration of the second pharmaceutical composition. As used herein the C_{max} provided by the administration of the second pharmaceutical composition may or may not include the plasma profile contribution of the first pharmaceutical composition. In embodiments, the administration of the second pharmaceutical composition does not include the plasma profile contribution of the first pharmaceutical composition. In embodiments, the first composition provides an *in vivo* plasma profile having a C_{max} that is more than about e.g., 60%, 70%, 80%, or 90% greater than the C_{max} provided by the administration of the second pharmaceutical composition.

[0165] In embodiments involving administration of a first pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt thereof, and a second pharmaceutical composition including gaboxadol or a pharmaceutically acceptable salt

thereof, the T_{max} of the first pharmaceutical composition is less than 3 hours. In embodiments, the T_{max} of the first pharmaceutical composition is less than 2.5 hours. In embodiments, the T_{max} of the first pharmaceutical composition is less than 2 hours. In embodiments, the T_{max} of the first pharmaceutical composition is less than 1.5 hours. In embodiments, the T_{max} of the first pharmaceutical composition is less than 1 hour.

[0166] In embodiments, the first and/or the second pharmaceutical compositions contain sub therapeutic dosages. A sub therapeutic dosage of gaboxadol is an amount of gaboxadol or a pharmaceutically acceptable salt thereof that is less than the amount required for a therapeutic effect. In embodiments, a sub therapeutic dosage is an amount of gaboxadol or a pharmaceutically acceptable salt thereof that alone may not provide improvement in at least one symptom of IBS, Crohn's disease, celiac disease ulcerative colitis, microscopic colitis or asthma, but is sufficient to maintain such improvement. In embodiments, the methods provide administering a first pharmaceutical composition that provides improvement in at least one symptom of IBS, Crohn's disease, celiac disease ulcerative colitis, microscopic colitis or asthma, and a second composition that maintains the improvement. In embodiments, after administration of the first pharmaceutical composition, the second pharmaceutical composition may provide a synergistic effect to improve at least one symptom of IBS, Crohn's disease, celiac disease ulcerative colitis, microscopic colitis or asthma. In embodiments the second pharmaceutical composition may provide a synergistic effect to improve at least one symptom of IBS, Crohn's disease, celiac disease ulcerative colitis, microscopic colitis or asthma.

[0167] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including a first pharmaceutical dosage including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement for more than 6 hours after administration and a second pharmaceutical composition including a sub therapeutic dosage of gaboxadol or a pharmaceutically acceptable salt thereof. In embodiments, provided herein are methods of treating Crohn's disease, celiac disease ulcerative colitis, or microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including a first pharmaceutical dosage including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement for more than 6 hours after administration and a second pharmaceutical composition including a sub therapeutic dosage of gaboxadol or a pharmaceutically acceptable salt thereof. In embodiments, provided herein are methods of treating asthma including administering to a patient in need thereof a pharmaceutical

composition including a first pharmaceutical dosage including gaboxadol or a pharmaceutically acceptable salt thereof wherein the composition provides improvement for more than 6 hours after administration and a second pharmaceutical composition including a sub therapeutic dosage of gaboxadol or a pharmaceutically acceptable salt thereof.

[0168] Administration of the first and second pharmaceutical compositions may be separated by an interval of time to achieve long-term improvement in at least one symptom of IBS, Crohn's disease, celiac disease ulcerative colitis, microscopic colitis or asthma. In embodiments, the first and second pharmaceutical composition may be administered 6 hours apart. In embodiments the first and second pharmaceutical composition may be administered 12 hours apart. In embodiments, the first and second pharmaceutical compositions may administered within, *e.g.*, 6 hours, 12 hours, 18 hours, 24 hours etc. In embodiments, the first and second pharmaceutical compositions may administered separated by at least, *e.g.*, 6 hours, 12 hours, 18 hours, 24 hours etc. In embodiments, improvement in at least one symptom of IBS, Crohn's disease, celiac disease ulcerative colitis, microscopic colitis or asthma for more than 8 hours after administration to the patient is provided. In embodiments, improvement for more than about, *e.g.*, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration to the patient is provided. In embodiments, improvement in at least one symptom of IBS, Crohn's disease, celiac disease ulcerative colitis, microscopic colitis or asthma for more than 8 hours after administration to the patient is provided. In embodiments, improvement for more than about, *e.g.*, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration to the patient is provided.

[0169] In embodiments, the first pharmaceutical composition and/or the second pharmaceutical composition include about 0.1 mg to about 40 mg gaboxadol or a pharmaceutically acceptable salt thereof. The amount of gaboxadol or a pharmaceutically acceptable salt thereof in the first pharmaceutical composition and the second pharmaceutical composition may be the same or different. In embodiments, the administration of the first and second pharmaceutical composition may provide a synergistic effect to improve at least one symptom of IBS, Crohn's disease, celiac disease ulcerative colitis, microscopic colitis or asthma.

[0170] In embodiments, the first and/or the second pharmaceutical composition include 0.1 mg to 25 mg, 0.1 mg to 20 mg, 0.1 mg to 15 mg, 0.5 mg to 25 mg, 0.5 mg to 20 mg, 0.5 to 15 mg, 1 mg to 25 mg, 1 mg to 20 mg, 1 mg to 15 mg, 1.5 mg to 25 mg, 1.5 mg to 20 mg, 1.5 mg to 15 mg, 2 mg to 25 mg, 2 mg to 20 mg, 2 mg to 15 mg, 2.5 mg to 25 mg, 2.5 mg to 20

mg, 2.5 mg to 15 mg, 3 mg to 25 mg, 3 mg to 20 mg, or 3 mg to 15 mg gaboxadol or a pharmaceutically acceptable salt thereof.

[0171] In embodiments, the first and/or the second pharmaceutical composition include 5 mg to 15 mg, 5 mg to 10 mg, 4 mg to 6 mg, 6 mg to 8 mg, 8 mg to 10 mg, 10 mg to 12 mg, 12 mg to 14 mg, 14 mg to 16 mg, 16 mg to 18 mg, or 18 mg to 20 mg gaboxadol or a pharmaceutically acceptable salt thereof.

[0172] In embodiments, the first and/or the second pharmaceutical composition include 0.1 mg, 0.25 mg, 0.5 mg, 1 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 7 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg, 17.5 mg, 20 mg gaboxadol or a pharmaceutically acceptable salt thereof or amounts that are multiples of such doses. In embodiments, the first pharmaceutical compositions include 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, or 20 mg gaboxadol or a pharmaceutically acceptable salt thereof. In embodiments, the second pharmaceutical compositions include 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, or 20 mg gaboxadol or a pharmaceutically acceptable salt thereof.

[0173] In embodiments, the first pharmaceutical composition provides a dissolution of at least about 80% within the first 20 minutes of administration to a patient in need thereof. In embodiments, the first pharmaceutical composition provides a dissolution of at least about, e.g., 85%, 90% or 95% within the first 20 minutes of administration to a patient in need thereof. In embodiments, the first pharmaceutical composition provides a dissolution of at least 80% within the first 10 minutes of administration to a patient in need thereof.

[0174] In embodiments, provided herein are methods of treating IBS including administering to a patient in need thereof a pharmaceutical composition including gaboxadol in combination with a second pharmaceutically active agent. In embodiments, provided herein are methods of treating Crohn's disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol in combination with a second pharmaceutically active agent. In embodiments, provided herein are methods of treating celiac disease including administering to a patient in need thereof a pharmaceutical composition including gaboxadol in combination with a second pharmaceutically active agent. In embodiments, provided herein are methods of treating ulcerative colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol in combination with a second pharmaceutically active agent. In embodiments, provided herein are methods of treating microscopic colitis including administering to a patient in need thereof a pharmaceutical composition including gaboxadol in combination with a second pharmaceutically active agent. In embodiments, provided herein are methods of treating

asthma including administering to a patient in need thereof a pharmaceutical composition including gaboxadol in combination with a second pharmaceutically active agent.

[0175] The second active agent may include an anti-diarrheal medication such as diphenoxylate/atropine, loperamide, paregoric, bismuth subsalicylate when symptoms include diarrhea. When constipation is a symptom the second active agent can include a laxative, e.g., bulk-forming agents, e.g., fiber; stool softeners, e.g., docusate; lubricants, e.g., mineral oil; hyperosmotic agents, e.g., sorbitol, mannitol, polyethylene glycol; stimulants, e.g., bisacodyl; or chloride channel activators, e.g., lubipostone. The second active agent can include an antispasmodic such as dicyclomine, promethazine, or peppermint oil. The second active agent can include an antidepressant, e.g., tricyclics such as amitriptyline, desipramine, doxepin, imipramine, nortryptyline, and protriptyline; SSRIs such as citalopram, escitalopram, fluoxetine, paroxetine, sertraline and vilazodone; SNRIs such as duloxetine, venlafaxine and desvenlafaxine; and NDRIs such as bupropion. The second active agent can include an anti-inflammatory such as an aminosalicylate, e.g., 4-aminosalicylic acid, balsazide, olsalazine, sulfasalazine or mesalazine; or a corticosteroid such as cortisol, cortisone, predisone, prednisolone, methylprednisolone, dexamethasone, betamethasone, triamcinolone or fludrocortisone acetate. The second active agent may include immunomodulators such as azathioprine, 6-mercaptopurine, cyclosporine A, methotrexate and tacrolimus. The second active agent may include anti-TNF antibodies such as certolizumab, adalimumab, infliximab or natalizumab. The second active agent may include cholestyramine. The second active agent may include an antibiotic such as penicillin G, ampicillin, amoxicillin, methicillin, nafcillin, oxacillin, cloxacillin, dicloxacillin, carbenicillin, mezlocillin, clavulanic acid, sulbactam, cefacetrile, cefadroxil, cephalexin, cefazolin, cefradine, loracarbef, cefoxitin, cefdinir, azithromycin, clarithromycin, erythromycin, fidaxomicin, sulfacetamide, sulfadiazine, sulfisoxazole, sulfamethoxazole, sulfadimethoxine sulfadoxine, lincomycin, clindamycin, streptomycin, kanamycin, gentamicin, doxycycline, chlortetracycline, minocycline, tetracycline, oxytetracycline, orchloramphenicol. The second active agent may include an antiemetic such as prochloperazine, dimenhydrate or meclizine. In asthma, the second active agent may include a corticosteroid such as beclomethasone, budesonide, flunisolide, fluticasone, mometasone, prednisone, prednisolone, methylprednisolone; or a leukotriene inhibitor such as ontelukast, zafirlukast, or zileuton; a beta-agonist such as albuterol, formoterol, metaproterenol, pirbuterol, or salmeterol; theophylline; Ipratropium bromide; tiotropium; cromolyn sodium;

omalizumab; or mepolizumab. The foregoing second active agents are representative and should not be considered a limiting.

[0176] Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of skill in the art to which the disclosure herein belongs.

[0177] The term "about" or "approximately" as used herein means within an acceptable error range for the particular value as determined by one of ordinary skill in the art, which will depend in part on how the value is measured or determined, i.e., the limitations of the measurement system. For example, "about" can mean within 3 or more than 3 standard deviations, per the practice in the art. Alternatively, "about" can mean a range of up to 20%, up to 10%, up to 5%, and/or up to 1% of a given value. Alternatively, particularly with respect to biological systems or processes, the term can mean within an order of magnitude, preferably within 5-fold, and more preferably within 2-fold, of a value.

[0178] "Improvement" refers to the treatment of IBS, Crohn's disease, celiac disease ulcerative colitis, microscopic colitis or asthma measured relative to at least one respective symptom.

[0179] "Improvement in one or more symptoms of IBS, Crohn's disease, celiac disease ulcerative colitis, microscopic colitis or asthma a day after administration" refers to improvement wherein the beneficial effect of at least one symptom lasts over a period of time, *e.g.*, 6 hours, 12 hours, 24 hours etc. "Improvement the next day" refers to improvement which occurs a day after administration of the active agent.

[0180] "PK" refers to the pharmacokinetic profile. C_{max} is defined as the highest plasma drug concentration estimated during an experiment (ng/ml). T_{max} is defined as the time when C_{max} is estimated (min). $AUC_{0-\infty}$ is the total area under the plasma drug concentration-time curve, from drug administration until the drug is eliminated (ng•hr/ml). The area under the curve is governed by clearance. Clearance is defined as the volume of blood or plasma that is totally cleared of its content of drug per unit time (ml/min).

[0181] "Treating" or "treatment" refers to alleviating or delaying the appearance of clinical symptoms of a disease or condition in a subject that may be afflicted with or predisposed to the disease or condition, but does not yet experience or display clinical or subclinical symptoms of the disease or condition. In certain embodiments, "treating" or "treatment" may refer to preventing the appearance of clinical symptoms of a disease or condition in a subject that may be afflicted with or predisposed to the disease or condition, but does not yet

experience or display clinical or subclinical symptoms of the disease or condition. "Treating" or "treatment" also refers to inhibiting the disease or condition, *e.g.*, arresting or reducing its development or at least one clinical or subclinical symptom thereof. "Treating" or "treatment" further refers to relieving the disease or condition, *e.g.*, causing regression of the disease or condition or at least one of its clinical or subclinical symptoms. The benefit to a subject to be treated may be statistically significant, mathematically significant, or at least perceptible to the subject and/or the physician. Nonetheless, prophylactic (preventive) and therapeutic (curative) treatment are two separate aspects of the disclosure herein.

[0182] "Pharmaceutically acceptable" refers to molecular entities and compositions that are "generally regarded as safe"-*e.g.*, that are physiologically tolerable and do not typically produce an allergic or similar untoward reaction, such as gastric upset and the like, when administered to a human. In embodiments, this term refers to molecular entities and compositions approved by a regulatory agency of the federal or a state government, as the GRAS list under section 204(s) and 409 of the Federal Food, Drug and Cosmetic Act, that is subject to premarket review and approval by the FDA or similar lists, the U.S. Pharmacopeia or another generally recognized pharmacopeia for use in animals, and more particularly in humans.

[0183] "Composition", "pharmaceutical composition", "therapeutic composition", "formulation", "pharmaceutical formulation" are used interchangeably herein. "Composition", "pharmaceutical composition", "therapeutic composition", "formulation", "pharmaceutical formulation" encompass dosage forms. Dosage forms can encompass unit doses.

[0184] "Effective amount" or "therapeutically effective amount" means a dosage sufficient to alleviate one or more symptoms of a disorder, disease, or condition being treated, e.g., IBS, Crohn's disease, celiac disease ulcerative colitis, microscopic colitis or asthma, or to otherwise provide a desired pharmacological and/or physiologic effect.

[0185] "Co-administered with", "in combination with", "a combination of", "administered along with", or "co-therapy", may be used interchangeably and mean that two or more agents are administered in the course of therapy. The agents may be administered together at the same time or separately in spaced apart intervals. The agents may be administered in a single dosage form or in separate dosage forms.

[0186] "Patient in need thereof" includes individuals that have been diagnosed IBS, Crohn's disease, celiac disease ulcerative colitis, microscopic colitis or asthma. The methods may be provided to any individual including, *e.g.*, wherein the patient is a neonate, infant, a pediatric

patient (6 months to 12 years), an adolescent patient (age 12-18 years) or an adult (over 18 years). "Patient" and "subject" are used interchangeably herein.

EXAMPLES

[0187] The Examples provided herein are included solely for augmenting the disclosure herein and should not be considered to be limiting in any respect.

Example 1

[0188] The following Example provides the plasma concentration profiles and dose proportionality of gaboxadol monohydrate following single oral doses ranging from 2.5 to 20 mg. The absolute bioavailability of gaboxadol monohydrate capsules ranging from 2.5 to 20 mg is also assessed.

[0189] This study was composed of separate groups of 10 healthy adult subjects (at least 4 of each gender) who participated in a 6-period, double-blind, randomized, crossover study designed to access the dose proportionality and absolute bioavailabilty of 5 single oral doses of gaboxadol across the dose range of 2.5 to 20 mg. The order in which the subjects received the 5 single oral doses of gaboxadol (2.5; 5; 10; 15; and 20 mg) was randomized within Treatment Periods 1 through 5. Each subject was expected to complete all 6 treatment periods and there was a washout of at least 4 days between each treatment period.

[0190] Each oral dosing within Treatment Periods consisted of 2 capsules of test drug taken simultaneously at each scheduled dosing. The treatment designations for the orally administered study drugs were as follows: Treatment A - one 2.5 mg gaboxadol capsule and 1 matching placebo capsule; Treatment B - one 5 mg gaboxadol capsule and 1 matching placebo capsule; Treatment C - one 10 mg gaboxadol capsule and 1 matching placebo capsule; Treatment D - one 15 mg gaboxadol capsule and 1 matching placebo capsule; and Treatment E - 20 mg gaboxadol (two 10 mg gaboxadol capsules). Subjects received their study drug after an overnight fast with 240 mL of water in the morning about 8:00 AM. Water was permitted *ad libitum* except within 1 hour prior to and after study drug administration. No food was allowed for 4 hours post dose.

[0191] For each subject in each treatment, plasma and urine samples were collected over 16 hours post-dosing for the determination of pharmacokinetic parameters (*e.g.*, AUC, C_{max}, T_{max}, apparent $t_{1/2}$, cumulative urinary excretion, renal clearance, clearance, and steady-state volume of distribution, as appropriate). AUC and C_{max} for gaboxadol were potency adjusted to facilitate comparison of pharmacokinetic data across studies. Table 1 provides the

individual potency-adjusted pharmacokinetic parameters of gaboxadol following single oral doses (2.5, 5, 10, 15, and 20 mg).

TABLE 1

Pharmacokinetic parameters for gaboxadol following oral and IV administration

Parameter	Geometric Mean (N=10)						
	2.5 mg	5 mg	10 mg Oral	10 mg I.V.	15 mg	20 mg	Slope (90 % CI) ††
$AUC_{0-\infty}$ (ng·hr/mL)	90	171	346	380	539	669	0.98 (0.95, 1.01)
C_{max} (ng/mL)†	61	110	232	212	382	393	0.95 (0.88, 1.02)
T_{max} (hr)‡	0.5	0.6	0.5	--	0.5	0.6	
Apparent $t_{1/2}$ (hr)§	1.5	1.5	1.6	1.5	1.5	1.6	
CL/F (mL/min)ɔ	461	488	476	438	469	499	
F_e (%)	43	45	53	53	50	53	
CL_R (mL/min)	196	222	250	208	234	265	
F (%) (90% CI)#	92% (0.86, 0.97)						

† C_{coi} (ng/mL) for 10 mg. IV.
‡ Median.
§ Harmonic Mean.
ɔ CL (mL/min) for 10 mg IV.
Bioavailability relative to 10 mg I.V. reference based on pooled dose-adjusted (to 10 mg) oral $AUC_{0-\infty}$ values.
†† Dose proportionality assessment of oral treatments only.

[0192] Figure 2 shows the arithmetic mean plasma concentration-time profiles of gaboxadol following single oral doses (2.5, 5, 10, 15, and 20 mg). The bioavailability of gaboxadol is approximately 92%. Plasma $AUC_{0-\infty}$ and C_{max} of gaboxadol show dose proportional increases and appear to be linear over the entire dose range examined, from of 2.5 to 20 mg. The time to peak plasma concentrations (T_{max} 30-60 min) and the half-life ($t_{½}$ of 1.5 h) for gaboxadol appear to be independent of dose across the gaboxadol dose range of 2.5 to 20 mg. The excretion of gaboxadol is mainly via urine, where 96.5% of the dose is recovered; 75% is recovered within 4 hours after administration.

Example 2

Assessment of Residual Effects Resulting from Gaboxadol Administration

[0193] This study was a double blind, double-dummy, randomized, active- and placebo-controlled, single dose, 3-period crossover study, followed by an open-label, single-dose, single period study in healthy elderly male and female subjects. Subjects were randomized to each of 3 treatments (Treatments A, B, and C) to be administered in a crossover manner over

the first 3 treatment periods. For Treatment A, subjects received a single dose of gaboxadol 10 mg; for Treatment B, subjects received a single dose of flurazepam 30 mg; and for Treatment C, subjects received a single dose of placebo. Doses were administered orally at bedtime on Day 1. Subjects were domiciled from early in the evening of dosing until ~36 hours post-dose (morning of Day 3) during each treatment period. The subjects who participated in treatment periods 1-3 participated in a fourth treatment period. In this period, a single dose of gaboxadol 10 mg (Treatment D) was administered orally in an open-label manner on the morning of Day 1 for PK of gaboxadol. There was at least a 14-day washout between the doses of consecutive treatment periods. Study participants included healthy, elderly male and female subjects between 65 and 80 years of age, with a Mini Mental Status 24, weighing at least 55 kg.

[0194] All subjects received 10 mg gaboxadol monohydrate capsules and 30 mg flurazepam (provided as 2 x 15 mg capsules), matching placebo was provided for both gaboxadol and flurazepam.

[0195] The primary endpoints evaluated included pharmacodynamics (measurement of psychomotor performance, memory, attention and daytime sleepiness the following pm dosing), gaboxadol pharmacokinetics, and safety. Gaboxadol (single dose 10 mg) did not show residual effect 9 hours post-dose on the primary endpoints Choice Reaction Time and Critical Flicker Fusion, whereas the active reference Flurazepam (30 mg single dose) showed significant effect on the same tests. In addition, gaboxadol did not show any signs of residual effects on other measurements applied in the study (Multiple Sleep Latency Test (MSLT); Digit symbol substitution test (DSST), Tracking, Memory tests, Body Sway, and Leeds Sleep Evaluation Questionnaire).

Example 3

Assessment of the Efficacy of Gaboxadol in Patients with Angelman syndrome

[0196] This study was designed to determine whether gaboxadol will lead to an improvement in key symptoms of Angelman syndrome (gross and fine motor function, sleep, and behavior problems) and related impact on daily life using questionnaires, diaries, or actimetry data. This multicenter, randomized, parallel (3-arm), double-blind, placebo-controlled trial enrolled 88 patients including adults (n=66) and adolescents (n=22) aged 13 to 49 years of age, diagnosed with Angelman syndrome. The study was designed to evaluate the safety and tolerability of gaboxadol from Baseline to Week 6 and Week 12 in subjects with Angelman syndrome across different dose levels and in 2 dosing schedules. The dosing schedules that

were assessed against placebo were once daily (QD): An evening dose titrated to the target dose of 15 mg unless not tolerated; and twice daily (BID): Evening and morning doses titrated to the target doses of 15 mg evening dose and 10 mg morning dose unless not tolerated. Accordingly, the three arms evaluated included (1) once-daily (QD) dose of gaboxadol at night (15 mg); (2) twice daily (BID) dose of gaboxadol (10 mg in the morning and 15 mg at night); and (3) placebo

[0197] The Clinical Global Impressions (Severity [CGI-S] and Improvement [CGI-I]) were used to assess the efficacy of gaboxadol in subjects. CGI-S scale assessed all sub-domains of Angelman syndrome (gross and fine motor ability, sleep, and adaptive behavior) plus globally by the investigator. On the CGI-S, significant changes for the QD (vs. Placebo) were observed for Stereotypic behavior 3.7 to 3.1 (3.3 to 3.6) and Hyperactivity 3.5 to 2.9 (3.1 to 3.0). The Clinical Global Impressions-Improvement (CGI-I) scale was used to assess all sub-domains of Angelman syndrome (gross and fine motor ability, sleep, and adaptive behavior) plus globally by the investigator and caregiver. CGI-I is a 7-point scale in which the investigator rates the improvement or worsening of symptoms compared to baseline. Once daily dosing (QD) resulted in a CGI-I of 3.0 vs. 3.8 in the placebo group ($p=0.0006$). The CGI-I, as assessed by clinicians, are provided in Table II. The data also shows significant results ($p=0.01$) in the pre-specified primary efficacy endpoint of Angelman syndrome in the combined treatment groups.

[0198] In addition, the number of responders (defined by a one point or greater improvement in the CGI-I scale) in overall symptoms in the once daily dose cohort (vs. placebo) was 70% (vs. 26%), increasing from 60% (vs. 22%) in the 25-49 year old, to 73% (vs. 27%) in the 18-24 year old, to 83% (vs. 29%) in the 13-17 year old cohort. Moreover, the percentage who were very much improved on CGI-I in the QD group vs placebo went from 20% (vs. 11%) to 27% (vs. 9%) to 33% (vs. 0%) progressing from the oldest to youngest cohorts. The improvement also increased with duration of treatment, comparing the 6-week to 12-week data.

Table II

	Placebo (N=29)	QD dosing (N=29)	BID dosing (N=29)	Combined (N=58)
6-week LS Mean	3.60 (0.15)	3.54 (0.16)	3.54 (0.16)	3.45 (0.12)
6-week LS Mean difference		-0.24 (0.21)	-0.06 (0.21)	-0.15 (0.18)
12-week LS Mean	3.79 (0.16)	3.00 (0.16)	3.58 (0.16)	3.29 (0.12)
12-week LS Mean difference		-0.78 (0.22)	-0.21 (0.22)	-0.49 (0.19)
P-value*		0.0006	0.3446	0.010

Note: Subjects are analyzed according to their randomized treatment. 2: CGI-I consists of 10 items. For improvement, scoring is: 1=very much improved, 2=much improved, 3=minimally improved, 4=no change, 5=minimally worse, 6=much worse, 7=very much worse. 3: A mixed model repeated measures (MMRM) analysis was performed including fixed effects for visit, treatment, age group 1 (adolescent vs. adult), and the visit by treatment interaction using a Unstructured covariance structure.
*Two-sided p-value for the difference of active treatment minus placebo.

[0199] The most notable change from patient sleep diaries was in the number of nights slept independently. In the QD dose cohort, one quarter of patients slept every night with parents, at 12 weeks, this had improved to only 1 in 5 nights; in the placebo group, the most effected quarter slept 3 of 4 nights with parents, which had improved to 2 of 4 nights at 12 weeks ($P<0.001$, Chi Square). The observed and change from baseline in total hours of sleep time at night (assessed from subject Sleep Diary) is provided in Table III.

Table III

	Placebo (N=29)	QD dosing (N=29)	BID dosing (N=29)	Combined (N=58)
6-week LS Mean sleep time	8.89 (1.4)	8.91 (1.5)	8.95 (1.1)	8.93 (1.3)
6-week LS Mean difference		0.14 (0.81)	0.30 (1.1)	0.22 (0.94)
12-week LS Mean sleep time	8.47 (1.4)	8.76 (1.2)	8.84 (1.1)	8.80 (1.1)
12-week LS Mean difference		-0.04 (1.1)	0.18 (0.97)	0.07 (1.0)

Note: Subjects are analyzed according to their randomized group. 2: Subject daily averages are calculated for Baseline, Week 6, and Week 12 visits using a window of 7 consecutive days prior to each visit. Summary statistics are reported using the daily average for each subject. 3: Total Sleep Time at night is defined from time of sleep onset to time of awakening. Daytime Sleepiness is duration of napping from the daytime sleep diary.

[0200] Of particular significance was that treatment-related gastrointestinal adverse events, including nausea, vomiting and abdominal pain, was observed in 6 of 29 placebo patients and 0 of 29 in the once daily gaboxadol group, consistent with improvement in gastrointestinal symptoms in this population ($P<0.01$; Chi-square). Gastrointestinal adverse events may be considered fundamental to the behavioral disturbances seen in autistic spectrum disorders, such as autism and Angelman syndrome. The incidences of treatment-related and treatment-

emergent Adverse Events were evaluated by system organ class with those related to gastrointestinal events are provided in Table IV.

Table IV

	Placebo (N=29)	QD dosing (N=29)	BID dosing (N=29)	Combined (N=58)
At least 1 Adverse Event	13 (45%)	18 (62%)	19 (66%)	37 (64%)
Gastrointestinal disorders	6 (20%)	0	4 (13.8%)	4 (6.9%)
Nausea	2 (6.9%)	0	2 (6.9%)	2 (3.4%)
Vomiting	3 (10.3%)	0	1 (3.4%)	1 (1.7%)
Diarrhea	2 (6.9%)	0	1 (3.4%)	1 (1.7%)
Abdominal Pain upper	1 (3.4%)	0	0	0
Retching	0	0	1 (3.4%)	1 (1.7%)

Note: Subjects were analyzed according to their actual treatment. 2: All adverse events are codes using MedDRA version 19.1. 3: A subject is counted only once within each system organ class and preferred term

Example 4

Prospective Assessment of the Efficacy of Gaboxadol in Patients with IBS

[0201] This study is designed to determine whether gaboxadol leads to an improvement in IBS. The primary objective of this study may be to evaluate the safety and tolerability from Baseline to Week 6 and Week 12 of gaboxadol in adult subjects with IBS across different dose levels and in two dosing schedules. The following dosing schedules may be tested against placebo: (1) Once daily (o.d.): An evening dose, titrated to the target dose of 15 mg unless not tolerated; and (2) Twice daily (b.i.d.): Evening and morning doses titrated to the target doses of 15 mg evening dose and 10 mg morning dose unless not tolerated.

[0202] The Safety endpoints that relate to this study may include: (1) Frequency and severity of adverse events (AEs) and serious adverse events; (2) Vital signs (weight, blood pressure, temperature); (3) Laboratory parameters (electrolytes, lipids, glucose, liver and pancreas function tests, hematology, creatinine).

[0203] The secondary objective of this study may include the identification of a set of parameters that may best characterize the efficacy of gaboxadol in adult IBS subjects for subsequent efficacy trials. These tests may be administered at four full day site visits (Screening, Baseline, Interim and End of Treatment) by an appropriately trained professional to provide the test to an adult IBS patient. Assessments may be based, in part, on patient's perception of symptoms.

[0204] This study may include three treatment groups. For example, a total of approximately 75 subjects may be enrolled and at the completion of the study, there may be approximately 25 subjects in each of the three treatment groups: 1) single evening dose 2) morning and evening dose and 3) placebo. All subjects may be up-titrated to the target dose unless this target dose is not tolerated (titration conventions described below). All subjects may receive treatment for a maximum of 12 weeks at their optimal tolerated dose.

[0205] Doses may be progressively increased in 5 mg increments (active or placebo) to a target dose of 3 capsules evening dose in schedule A and B, and 2 capsules morning dose in schedule B. Each dose escalation may be performed after adequate tolerability has been assessed by caregiver and investigator. For example, treatment initiation at Day 1 with 1 capsule (active (Act) or placebo (Plc)) in the evening. Then target up-titration may begin at Day 3 (window + 2 days): If no adverse event (AE) related to the study drug is observed by caregiver and/or the investigator, another capsule (active or placebo) is added in the evening. Again at Day 7 (window + 2 days), Day 10 (window + 2 days and Day 14 (window + 2 days) if no AE related to the study drug is observed by caregiver and/or the investigator, another capsule (active or placebo) may be added in the morning. Table V below provides a graphic illustration of the titration schedule.

Table V. Titration Schedule

Schedule/Time		Days 1 to 2	Days 3 to 6	Days 7 to 9	Days 10 to 13	Day 14*
Schedule A	Evening	5 mg 1 Capsule	10 mg 2 Capsules	15 mg 3 Capsules	15 mg 3 Capsules	15 mg 3 Capsules
	Morning	None	None	None	Placebo 1 Capsule	Placebo 2 Capsules
Schedule B	Evening	5 mg 1 Capsule	10 mg 2 Capsules	15 mg 3 Capsules	15 mg 3 Capsules	15 mg 3 Capsules
	Morning	None	None	None	5 mg 1 Capsule	10 mg 2 Capsules
Schedule C	Evening	Placebo 1 Capsule	Placebo 2 Capsules	Placebo 3 Capsules	Placebo 3 Capsules	Placebo 3 Capsules
	Morning	None	None	None	Placebo 1 Capsule	Placebo 2 Capsules

* To end of study treatment period

[0206] Slowed up-titration or delayed up-titration will be acceptable if tolerability does not allow immediate further dose-escalation at any of the above detailed days (3, 7, 10, 14). Down-titration in the case tolerability is not acceptable (e.g., somnolence, dizziness, change in behavior) after a previous up-titration step or during the course of the 12 week treatment, dose can be reduced to the previous level or even further. However, once a tolerable dose has been reached, it shall remain constant for the duration of the treatment period. Once a target dose is achieved the treatment may continue. For example, at Day 14: Earliest day the target dose can be reached (2 capsules in the morning and 3 in the evening) the subject may be kept stable until End of Treatment visit (week 12) unless intolerability requires down-titration.

[0207] All subjects will be screened for participation in the study up to 28 days prior to the first dose administration. Inclusion criteria may include one or more of the following: (1) Age ≥ 18 years, ≤ 40 years; (2) Must possess a clinical diagnosis of IBS. Descriptive statistics may be used to summarize all primary and secondary endpoints as well as baseline variables, by treatment group. For continuous variables, n, number of missing values, mean, standard deviation, median, minimum, and maximum will be provided. For categorical variables, frequency and percentage will be presented for each category. Confidence intervals (CI) will be provided where meaningful. All CIs will be two-sided 95% confidence intervals.

[0208] Primary outcome measures:The relief of irritable bowel syndrome symptoms will be used to measure the effectiveness of gaboxadol. The parameters used to evaluate the effectiveness of gaboxadol will include i) Abdominal pain (0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = severe pain); ii) Frequency of the pain (# of pains per day); iii) Abdominal discomfort (0 = No discomfort,1 = mild,2 = moderate,3 = severe); iv) Frequency of discomfort (# of discomfort per day); v) # of stools per day; vi) Form (appearance) of stool (0 = Normal, 1 = soft pieces with clear-cut edges, 2 = mushy, 3 = watery). Secondary outcome measures: The following will be documented: constipation, headache, dizzy, hypertension, chest pain, abdominal pain, flatus, anxiety, insomnia, nausea, fever, fatigue, and muscle pain.

Example 5

Prospective Assessment of the Efficacy of Gaboxadol in Patients with Asthma

[0209] This study is designed to determine whether gaboxadol leads to an improvement in asthma. The primary objective of this study may be to evaluate the safety, tolerability and efficacy from Baseline to Week 6 and Week 12 of gaboxadol in adult subjects with asthma across different dose levels and in two dosing schedules. The following dosing schedules may be tested against placebo: (1) Once daily (o.d.): An evening dose, titrated to the target dose of 15 mg unless not tolerated; and (2) Twice daily (b.i.d.): Evening and morning doses titrated to the target doses of 15 mg evening dose and 10 mg morning dose unless not tolerated.

[0210] The Safety endpoints that relate to this study may include: (1) Frequency and severity of adverse events (AEs) and serious adverse events; (2) Vital signs (weight, blood pressure, temperature); (3) Laboratory parameters (electrolytes, lipids, glucose, liver and pancreas function tests, hematology, creatinine).

[0211] The secondary objective of this study may include the identification of a set of parameters that may best characterize the efficacy of gaboxadol in adult asthma subjects for

subsequent efficacy trials. These tests may be administered at four full day site visits (Screening, Baseline, Interim and End of Treatment) by an appropriately trained professional to provide the test to an adult asthma patient. Assessments may be based, in part, on patient's perception of symptoms.

[0212] This study may include three treatment groups. For example, a total of approximately 75 subjects may be enrolled and at the completion of the study, there may be approximately 25 subjects in each of the three treatment groups: 1) single evening dose 2) morning and evening dose and 3) placebo. All subjects may be up-titrated to the target dose unless this target dose is not tolerated (titration conventions described below). All subjects may receive treatment for a maximum of 12 weeks at their optimal tolerated dose.

[0213] Doses may be progressively increased in 5 mg increments (active or placebo) to a target dose of 3 capsules evening dose in schedule A and B, and 2 capsules morning dose in schedule B. Each dose escalation may be performed after adequate tolerability has been assessed by caregiver and investigator. For example, treatment initiation at Day 1 with 1 capsule (active (Act) or placebo (Plc)) in the evening. Then target up-titration may begin at Day 3 (window + 2 days): If no adverse event (AE) related to the study drug is observed by caregiver and/or the investigator, another capsule (active or placebo) is added in the evening. Again at Day 7 (window + 2 days), Day 10 (window + 2 days and Day 14 (window + 2 days) if no AE related to the study drug is observed by caregiver and/or the investigator, another capsule (active or placebo) may be added in the morning. Table VI below provides a graphic illustration of the titration schedule.

Table VI. Titration Schedule

Schedule/Time		Days 1 to 2	Days 3 to 6	Days 7 to 9	Days 10 to 13	Day 14*
Schedule A	**Evening**	5 mg 1 Capsule	10 mg 2 Capsules	15 mg 3 Capsules	15 mg 3 Capsules	15 mg 3 Capsules
	Morning	None	None	None	Placebo 1 Capsule	Placebo 2 Capsules
Schedule B	**Evening**	5 mg 1 Capsule	10 mg 2 Capsules	15 mg 3 Capsules	15 mg 3 Capsules	15 mg 3 Capsules
	Morning	None	None	None	5 mg 1 Capsule	10 mg 2 Capsules
Schedule C	**Evening**	Placebo 1 Capsule	Placebo 2 Capsules	Placebo 3 Capsules	Placebo 3 Capsules	Placebo 3 Capsules
	Morning	None	None	None	Placebo 1 Capsule	Placebo 2 Capsules

* To end of study treatment period

[0214] Slowed up-titration or delayed up-titration will be acceptable if tolerability does not allow immediate further dose-escalation at any of the above detailed days (3, 7, 10, 14). Down-titration in the case tolerability is not acceptable (e.g., somnolence, dizziness, change in behavior) after a previous up-titration step or during the course of the 12 week treatment, dose can be reduced to the previous level or even further. However, once a tolerable dose has been reached, it shall remain constant for the duration of the treatment period. Once a target dose is achieved the treatment may continue. For example, at Day 14: Earliest day the target

dose can be reached (2 capsules in the morning and 3 in the evening) the subject may be kept stable until End of Treatment visit (week 12) unless intolerability requires down-titration.

[0215] All subjects will be screened for participation in the study up to 28 days prior to the first dose administration. Inclusion criteria may include one or more of the following: (1) Age $\geq$ 18 years, $\leq$ 40 years; (2) Must possess a clinical diagnosis of IBS. Descriptive statistics may be used to summarize all primary and secondary endpoints as well as baseline variables, by treatment group. For continuous variables, n, number of missing values, mean, standard deviation, median, minimum, and maximum will be provided. For categorical variables, frequency and percentage will be presented for each category. Confidence intervals (CI) will be provided where meaningful. All CIs will be two-sided 95% confidence intervals.

[0216] Primary outcome measures: Difference between study arms in the change in asthma severity as measured by the Composite Asthma Severity Index (CASI). Secondary outcome measures: change in Forced Expiratory Volume (FEV1), mean change in number of day time symptom scores, mean change in number of night time symptoms, mean change in the number of daily puffs/inhalations of short-acting beta-agonist (SABA) rescue medication, mean change in daily doses of inhaled glucocorticoids taken (μg/day), mean change in the percentage of patients with an asthma exacerbation.

[0217] Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments described herein. Such equivalents are intended to be encompassed by the claims.

What is claimed is:

1. A method of treating irritable bowel syndrome comprising administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof, wherein the method provides improvement in one or more symptoms of irritable bowel syndrome in the patient.

2. The method of claim 1, wherein the improvement is provided for more than 6 hours after administration.

3. The method of claim 1, wherein the patient is administered a composition comprising about 1 mg to about 15 mg gaboxadol or a pharmaceutically acceptable salt thereof.

4. The method of claim 1, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 50%.

5. The method of claim 1, wherein the AUC_{6-12} of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is less than 75% of the administered dose.

6. The method of claim 1, wherein the method provides improvement in at least one symptom selected from the group consisting of cramping, repeated abdominal pain, bloating, diarrhea, and constipation.

7. The method of claim 2, wherein the composition provides improvement in the patient for at least 12 hours.

8. A method of treating irritable bowel syndrome comprising administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.

9. A method of treating irritable bowel syndrome comprising administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.

10. A method of treating Crohn's disease comprising administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof, wherein the method provides improvement in one or more symptoms of Crohn's disease in the patient.

11. The method of claim 10, wherein the improvement is provided for more than 6 hours after administration.

12. The method of claim 10, wherein the patient is administered a composition comprising about 1 mg to about 15 mg gaboxadol or a pharmaceutically acceptable salt thereof.

13. The method of claim 10, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 50%.

14. The method of claim 10, wherein the AUC_{6-12} of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is less than 75% of the administered dose.

15. The method of claim 10, wherein the method provides improvement in at least one symptom selected from the group consisting of diarrhea, cramping, abdominal pain, anemia, fever and nausea.

16. The method of claim 11, wherein the composition provides improvement in the patient for at least 12 hours.

17. A method of treating Crohn's disease comprising administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method

provides an *in vivo* plasma profile comprising a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.

18. A method of treating Crohn's disease comprising administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.

19. A method of treating celiac disease comprising administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof, wherein the method provides improvement in one or more symptoms of celiac disease in the patient.

20. The method of claim 19, wherein the improvement is provided for more than 6 hours after administration.

21. The method of claim 19, wherein the patient is administered a composition comprising about 1 mg to about 15 mg gaboxadol or a pharmaceutically acceptable salt thereof.

22. The method of claim 19, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 50%.

23. The method of claim 19, wherein the AUC_{6-12} of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is less than 75% of the administered dose.

24. The method of claim 19, wherein the method provides improvement in at least one symptom selected from the group consisting of bloating, chronic diarrhea, constipation, gas, nausea, pale, foul smelling stools, stomach pain and malabsorption of nutrients, delayed puberty, failure to thrive in infants, slowed growth and weight loss.

25. The method of claim 20, wherein the composition provides improvement in the patient for at least 12 hours.

26. A method of treating celiac disease comprising administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.

27. A method of treating celiac disease comprising administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.

28. A method of treating ulcerative colitis comprising administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof, wherein the method provides improvement in one or more symptoms of ulcerative colitis in the patient.

29. The method of claim 28, wherein the improvement is provided for more than 6 hours after administration.

30. The method of claim 28, wherein the patient is administered a composition comprising about 1 mg to about 15 mg gaboxadol or a pharmaceutically acceptable salt thereof.

31. The method of claim 28, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 50%.

32. The method of claim 28, wherein the AUC_{6-12} of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is less than 75% of the administered dose.

33. The method of claim 28, wherein the method provides improvement in at least one symptom selected from the group consisting of urgent need to have a bowel movement, bloody bowel movements, fever, severe abdominal cramping, fatigue, nausea, loss of appetite, weight loss, anemia, joint pain, and rashes.

34. The method of claim 29, wherein the composition provides improvement in the patient for at least 12 hours.

35. A method of treating celiac disease comprising administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.

36. A method of treating celiac disease comprising administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.

37. A method of treating microscopic colitis comprising administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof, wherein the method provides improvement in one or more symptoms of microscopic colitis in the patient.

38. The method of claim 37, wherein the improvement is provided for more than 6 hours after administration.

39. The method of claim 37, wherein the patient is administered a composition comprising about 1 mg to about 15 mg gaboxadol or a pharmaceutically acceptable salt thereof.

40. The method of claim 37, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 50%.

41. The method of claim 37, wherein the AUC_{6-12} of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is less than 75% of the administered dose.

42. The method of claim 37, wherein the method provides improvement in at least one symptom selected from the group consisting of chronic, watery, non-bloody diarrhea, a strong urgency to have a bowel movement, pain, cramping, bloating, weight loss, nausea, and fecal incontinence.

43. The method of claim 38, wherein the composition provides improvement in the patient for at least 12 hours.

44. A method of treating microscopic colitis comprising administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.

45. A method of treating microscopic colitis comprising administering to a patient in need thereof gaboxadol or a wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng•hr/ml and wherein the method provides improvement in the patient for more than pharmaceutically acceptable salt thereof 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.

46. A method of treating asthma comprising administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof, wherein the method provides improvement in one or more symptoms of asthma in the patient.

47. The method of claim 46, wherein the improvement is provided for more than 6 hours after administration.

48. The method of claim 46, wherein the patient is administered a composition comprising about 1 mg to about 15 mg gaboxadol or a pharmaceutically acceptable salt thereof.

49. The method of claim 46, wherein the *in vivo* plasma profile of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is reduced by more than 50%.

50. The method of claim 46, wherein the AUC_{6-12} of the patient 6 hours after administration of the gaboxadol or pharmaceutically acceptable salt thereof is less than 75% of the administered dose.

51. The method of claim 46, wherein the method provides improvement in at least one symptom selected from the group consisting of wheezing, chest tightness, shortness of breath, and coughing.

52. The method of claim 47, wherein the composition provides improvement in the patient for at least 12 hours.

53. A method of treating asthma comprising administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a C_{max} less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.

54. A method of treating asthma comprising administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an *in vivo* plasma profile comprising a AUC_{6-12} of less than about 900 ng•hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.

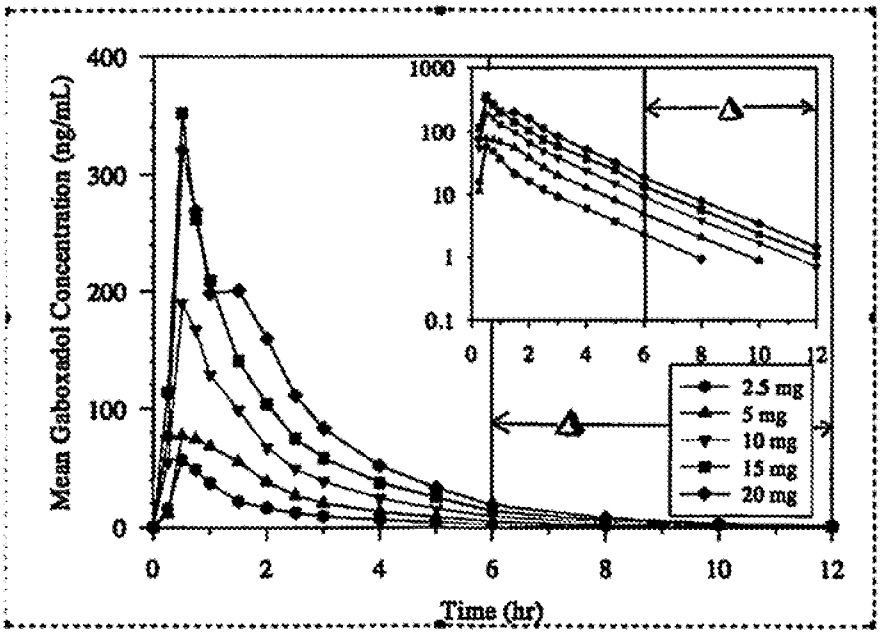
Mean Gaboxadol Concentration (ng/mL)
Time (hr)
2.5 mg
5 mg
10 mg
15 mg
20 mg

FIG. 1

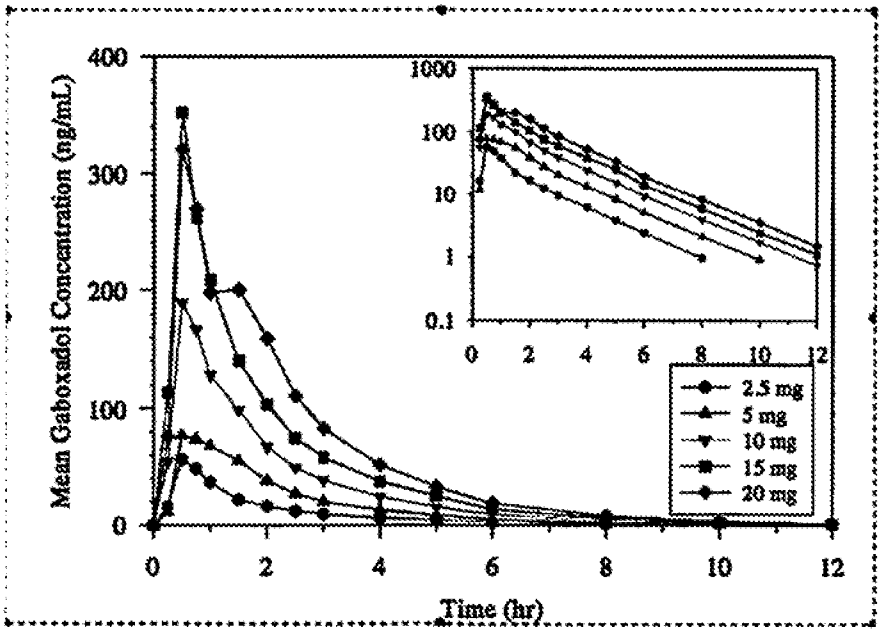
Mean Gaboxadol Concentration (ng/mL)
Time (hr)
2.5 mg
5 mg
10 mg
15 mg
20 mg

FIG. 2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/047673

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 31/437; A61K 31/00; A61K 31/4353; A61P 1/00 (2019.01)
CPC - A61K 31/437; A61K 31/00; A61K 31/4353; A61P 1/00 (2019.08)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 514/1; 514/300; 514/302 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2017/0014393 A1 (OVID THERAPEUTICS INC) 19 January 2017 (19.01.2017) entire document	1-9
A	US 2007/0203216 A1 (EBERT et al) 30 August 2007 (30.08.2007) entire document	1-9
A	WO 2006/102093 A1 (TRANSFORM PHARMACEUTICALS INC) 28 September 2006 (28.09.2006) entire document	1-9

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
05 December 2019	23 DEC 2019
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/047673

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
See extra sheet(s).

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-9

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/047673

Continued from Box No. III Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees need to be paid.

Group I: Claims 1-9 are drawn to methods of treating irritable bowel syndrome.

Group II: 10-18 are drawn to methods of treating Crohn's disease.

Group III: Claims 19-27, 35, and 36 are drawn to methods of treating celiac disease.

Group IV: Claims 28-34 and 37-45 are drawn to methods of treating colitis.

Group V: Claims 46-54 are drawn to methods of treating asthma.

The inventions listed in Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The special technical features of Group I, methods of treating irritable bowel syndrome, are not present in Groups II-V; the special technical features of Group II, methods of treating Crohn's disease, are not present in Groups I and III-V; the special technical features of Group III, methods of treating celiac disease, are not present in Groups I, II, IV, and V; the special technical features of Group IV, methods of treating colitis, are not present in Groups I-III and V; and the special technical features of Group V, methods of treating asthma, are not present in Groups I-IV.

Groups I-V share the technical features of a method of treating a condition comprising administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof, wherein the method provides improvement in one or more symptoms of the condition in the patient; wherein the method provides an in vivo plasma profile comprising a Cmax less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof; and wherein the method provides an in vivo plasma profile comprising a AUC6-12 of less than about 900 ng*hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof. However, these shared technical features do not represent a contribution over the prior art.

Specifically, US 2017/0014393 A1 to Ovid Therapeutics Inc. teaches a method of treating a condition (Abstract) comprising administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof, wherein the method provides improvement in one or more symptoms of the condition in the patient (Para. [0009], Methods of treating a developmental disorder described herein include administering to a patient in need thereof about 0.05 mg to about 30 mg gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides improvement in next day functioning); wherein the method provides an in vivo plasma profile comprising a Cmax less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof (Para. [0009], Methods of treating a developmental disorder are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an in vivo plasma profile including a Cmax less than about 400 ng/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof.); and wherein the method provides an in vivo plasma profile comprising a AUC6-12 of less than about 900 ng*hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof (Para. [0009], Methods of treating a developmental disorder are described herein which include administering to a patient in need thereof gaboxadol or a pharmaceutically acceptable salt thereof wherein the method provides an in vivo plasma profile comprising a AUC6-12 of less than about 900 ng·hr/ml and wherein the method provides improvement in the patient for more than 6 hours after administration of the gaboxadol or a pharmaceutically acceptable salt thereof).

The inventions listed in Groups I-V therefore lack unity under Rule 13 because they do not share a same or corresponding special technical feature.