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AAI is offering career services to both job seekers and employers through a Jobs Board free to meeting registrants and exhibitors at www.immunology2019.org/jobs-board.

Job Seekers!
Whatever your career stage, use this career service at IMMUNOLOGY 2019™ to enhance your professional development.

- **Job Postings**
  Review the online AAI Jobs Board to identify postings you wish to pursue. View new Advance Postings through April 26. Watch for additional On-site Postings in the Exhibit Hall.

- **Direct Access to Recruiters**
  Job postings will include recruiters’ e-mail addresses so that you can contact them directly.

Employers!
Advertise your position on the virtual Jobs Board located on the IMMUNOLOGY 2019™ website. By including a contact email, you will receive inquiries directly.

- **Advance Postings**
  Postings will be accepted as of February 20 via a web submission form and will remain online until the end of the meeting. Employers must be registered participants or exhibitors of IMMUNOLOGY 2019™ at the time of submission. Advance Postings must be submitted to AAI by April 26, 2019.

- **On-site Postings**
  After April 26, 2019, employers may still advertise a job on the IMMUNOLOGY 2019™ Jobs Board by visiting the AAI Office in the San Diego Convention Center between 9:00 AM and 5:00 PM. Ads submitted on-site will be posted on the Jobs Board in the Exhibit Hall.

Save Thousands of Dollars in Recruiting Expenses
Take advantage of this complimentary hiring opportunity at IMMUNOLOGY 2019™.
To register for the meeting, visit www.immunology2019.org/register.
INDICATION
TAKHZYRO is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients ≥12 years of age.

IMPORTANT SAFETY INFORMATION

Hypersensitivity reactions have been observed. In case of a severe hypersensitivity reaction, discontinue TAKHZYRO administration and institute appropriate treatment.

Adverse Reactions: The most commonly observed adverse reactions (≥10% and higher than placebo) associated with TAKHZYRO were injection site reactions consisting mainly of pain, erythema, and bruising at the injection site; upper respiratory infection; headache; rash; myalgia; dizziness; and diarrhea. Less common adverse reactions observed included elevated levels of transaminases; one patient discontinued the trial for elevated transaminases.

Use in Specific Populations: The safety and efficacy of TAKHZYRO in pediatric patients <12 years of age have not been established.

No data are available on TAKHZYRO in pregnant women. No data are available on the presence of lanadelumab in human milk or its effects on breastfed infants or milk production.

To report SUSPECTED ADVERSE REACTIONS, contact Dyax Corp. (a wholly-owned, indirect subsidiary of Shire plc) at 1-800-828-2088, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Brief Summary of safety information on the following page and full Prescribing Information at www.TAKHZYRO.com.

INDICATION
TAKHZYRO is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients ≥12 years of age.

REIMAGINE THE WAY YOU TREAT HAE

TAKHZYRO—a first-of-its-kind mAb preventive treatment

Rediscover prevention
- In the largest prevention study in HAE (N=125 patients ≥12 years of age) with the longest active treatment duration (26 weeks), the mean monthly attack rate was significantly lower for TAKHZYRO 300 mg every 2 weeks (0.26; n=27) vs placebo (1.97; n=41)**

Rethink dosing and administration
- One subcutaneous self-injection every 2 weeks†

Refine the approach
- The first and only mAb for HAE, TAKHZYRO inhibits plasma kallikrein activity

References:
1. TAKHZYRO (lanadelumab-flyo) [prescribing information]. Lexington, MA: Shire LLC; 2018.
Warning and Precautions

Hypersensitivity Reactions

Hypersensitivity reactions have been observed. In case of a severe hypersensitivity reaction, discontinue TAKHZYRO administration and institute appropriate treatment.

Adverse Reactions

The safety of TAKHZYRO is primarily based on a 26-week, randomized, double-blind, parallel-group and placebo-controlled study (Trial 1) in 125 patients with Type I or II hereditary angioedema (HAE). Eligible patients were also able to participate in an open-label angioedema extension study (Trial 2) up to 130 weeks. In Trial 1, a total of 84 patients with HAE aged 12 years and older received at least one dose of TAKHZYRO. Overall, 70% of patients were female and 90% of patients were Caucasian with a mean age of 41 years. The proportion of patients who discontinued the study drug prematurely due to adverse events was 1.2% for TAKHZYRO-treated patients and 4.9% for placebo-treated patients. No deaths occurred in the trial.

The safety profile of TAKHZYRO was generally similar across all subgroups of patients, including analysis by age, sex, and geographic region. Table 1 shows adverse reactions occurring in ≥10% of patients in any TAKHZYRO treatment group that also occurred at a higher rate than in the placebo treatment group in Trial 1.

Table 1. Adverse Reactions Observed in ≥10% of Patients Treated with TAKHZYRO in Trial 1

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Placebo (N=41)</th>
<th>TAKHZYRO 150 mg qwks (N=28)</th>
<th>TAKHZYRO 300 mg qwks (N=29)</th>
<th>TAKHZYRO 300 mg q2wks (N=27)</th>
<th>Total (N=84)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site reactions</td>
<td>14 (34)</td>
<td>16 (57)</td>
<td>13 (45)</td>
<td>15 (56)</td>
<td>44 (52)</td>
</tr>
<tr>
<td>Upper respiratory infection</td>
<td>13 (32)</td>
<td>3 (11)</td>
<td>9 (31)</td>
<td>12 (44)</td>
<td>24 (29)</td>
</tr>
<tr>
<td>Headache</td>
<td>9 (22)</td>
<td>3 (11)</td>
<td>6 (21)</td>
<td>9 (33)</td>
<td>18 (21)</td>
</tr>
<tr>
<td>Rash</td>
<td>2 (5)</td>
<td>2 (7)</td>
<td>3 (10)</td>
<td>1 (4)</td>
<td>6 (7)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>0</td>
<td>1 (4)</td>
<td>0</td>
<td>3 (11)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>0</td>
<td>1 (4)</td>
<td>3 (10)</td>
<td>1 (4)</td>
<td>5 (6)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (5)</td>
<td>3 (11)</td>
<td>0</td>
<td>1 (4)</td>
<td>4 (5)</td>
</tr>
</tbody>
</table>

N=number of patients; n=number of patients experiencing the event; qwks=every 4 weeks; q2wks=every 2 weeks; qwk=every 1 week

Injection site reactions includes: pain, erythema, bruising, hematoma, hemorrhage, pruritus, swelling, induration, paresthesia, reaction, warmth, edema and rash.

Includes upper respiratory infection, viral upper respiratory infection

Includes headache, tension headache, sinus headache

Includes rash, rash maculopapular, rash erythematosus

Injection site reactions primarily consisted mainly of pain, erythema, and bruising at the injection site. There was no meaningful difference in injection site reactions with self-administration.

Less Common Adverse Reactions

Other adverse reactions that occurred at a higher incidence in TAKHZYRO-treated patients compared to placebo include hypersensitivity (1% vs 0%), increased aspartate transaminase (2% vs 0%), and increased alanine transaminase (2% vs 0%). Safety data from the ongoing open-label extension study, consisting of 109 rollover patients from Trial 1 and 103 non-roller HAE patients, is consistent with controlled safety data from Trial 1.

Laboratory Abnormalities

Transaminase elevations

During the placebo-controlled treatment period in Trial 1, the number of TAKHZYRO-treated patients with maximum transaminase (ALT or AST) levels >5xULN or >10xULN was 1 (1.2%), 3 (10%), 3 (10%); >10xULN was 1 (1.2%), 3 (10%), 3 (10%); >5xULN was 1 (1.2%), 3 (10%), 3 (10%); >3xULN was 1 (1.2%), 3 (10%), 3 (10%); >2xULN was 1 (1.2%), 3 (10%), 3 (10%); >1xULN was 1 (1.2%), 3 (10%), 3 (10%)

IMMUNOCOMPETENCY

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease.

For these reasons, comparison of the incidence of antibodies to lanadelumab-flyo in the study described below with the incidence of antibodies in other studies or to other products may be misleading.

In Trial 1, 12% (10/84) lanadelumab-flyo treated and 2 (5%) placebo-treated patients had at least 1 anti-drug antibody (ADA)-positive sample during the treatment period; antibody titers were low (range: ≥20 to 1280). The ADA response observed was transient in 2/10 lanadelumab-flyo and 1/2 placebo-treated patients.

Pre-existing low titer antibodies were observed in 3 lanadelumab-flyo-treated patients and 1 placebo-treated patient with ADAs. Two patients receiving 150 mg q4wks had low titer antibodies classified as neutralizing. The development of ADA including neutralizing antibodies against lanadelumab-flyo did not appear to adversely affect pharmacokinetics (PK), pharmacodynamics (PD), safety or clinical response.

Drug Interactions

Drug-Laboratory Test Interactions

Coagulation tests TAKHZYRO can increase activated partial thromboplastin time (aPTT) due to an interaction of TAKHZYRO with the aPTT assay. The reagents used in the aPTT laboratory test initiate intrinsic coagulation through the activation of plasma kallikrein in the contact system. Inhibition of plasma kallikrein by TAKHZYRO can increase aPTT in this assay. In Trial 1, prolongation of aPTT (>1xULN) was observed at one or more time points in 3, 9, and 11 patients treated with TAKHZYRO 150 mg qwks, 300 mg qwks, and 300 mg q2wks, respectively, compared to 5 placebo-treated patients. Only one patient in the 300 mg q2wks treatment group experienced transient aPTT prolongation >1xULN which was compounded by ongoing heparin therapy. None of the increases in aPTT in patients treated with TAKHZYRO were associated with abnormal bleeding adverse events. There were no differences in INR values between treatment groups.

Use in Specific Populations

Pregnancy

There are no available data on TAKHZYRO use in pregnant women to inform any drug associated risks. Monoclonal antibodies such as lanadelumab-flyo are transported across the placenta during the third trimester of pregnancy; therefore, potential effects on a fetus are likely to be greater during the third trimester of pregnancy. An enhanced pre- and postnatal development (ePPND) study conducted in pregnant monkeys at doses resulting in exposures of up to 33 times the exposure observed in humans revealed no evidence of harm to the developing fetus. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Lactation

There are no data on the presence of lanadelumab-flyo in human milk, its effects on the breastfed infant, or its effects on milk production. Lanadelumab-flyo was detected in the milk of lactating cynomolgus monkeys at approximately 0.2% of the maternal plasma concentration. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TAKHZYRO and any potential adverse effects on the breastfed infant from TAKHZYRO or from the underlying maternal condition.

Pediatric Use

The safety and efficacy of TAKHZYRO were evaluated in a subgroup of patients (N=10) aged 12 to <18 years in Trial 1. Results of the subgroup analysis by age were consistent with overall study results (see Adverse Reactions (6.1), Clinical Pharmacology (12.3) and Clinical Trials (14)). An additional 13 adolescent patients aged 12 to <18 years were enrolled in the open-label extension study. The safety and efficacy of TAKHZYRO in pediatric patients <12 years of age have not been established.

Geriatric Use

The safety and efficacy of TAKHZYRO were evaluated in a subgroup of patients (N=5) aged ≥65 years in Trial 1. Results of the subgroup analysis by age were consistent with overall study results.

Patient Counseling Information

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use). Inform patients of the risks and benefits of TAKHZYRO before prescribing or administering to the patient.

Hypersensitivity

Advise patients to seek immediate medical attention if they experience any symptoms of serious hypersensitivity reactions [see Warnings and Precautions (5.1)].

Self-administration:

- Ensure that the patient/caregiver receives clear instructions and training on subcutaneous administration and has demonstrated the ability to perform a subcutaneous injection.
- Instruct patients or caregivers in the technique of proper syringe and needle disposal, and advise them not to reuse these items. Instruct patients to dispose of needles and syringes in a puncture-resistant container.

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Pattern recognition receptors (PRRs) recognize a wide variety of ligands, called pathogen-associated molecular patterns (PAMPs), discriminating gram-positive and gram-negative bacteria from fungi and other pathogens. InvivoGen offers the most comprehensive choice of ligands, known to activate specific PRRs, that can serve as controls in genetic and pharmaceutical studies on PRRs. InvivoGen strives to provide PRR ligands of the highest quality. We thoroughly validate our ligands using proprietary PRR reporter cells to ensure high quality and lot-to-lot reproducibility. Our sound technical support is committed to provide assistance for any queries.

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