Filed on behalf of: Amneal Pharmaceuticals, Inc.
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AMNEAL PHARMACEUTICALS, INC. AND KASHIV BIOSCIENCES,
Petitioner,

v.

GENENTECH, INC.,
Patent Owner.

Case No. IPR2026-00260
Patent No. 12,030,959

PETITION FOR INTER PARTES REVIEW OF U.S. PATENT NO. 12,030,959

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I. INTRODUCTION

Amneal Pharmaceuticals, Inc. and Kashiv BioSciences ("Petitioner") respectfully requests *inter partes* review of claims 1-29 of US12,030,959 ("*US959*" EX1001), assigned to Novartis AG and Genentech, Inc. (collectively "Genentech" or "PO"). Amneal is a United States company, incorporated in Delaware, and employs over 2,400 people in the United States. Kashiv, while an Indian company, has invested in manufacturing operations in the United States, employing around 270 people.

Omalizumab, which Genentech markets under the trade name XOLAIR, is an antibody that inhibits the function of IgE, a type of antibody that plays a key role in mediating the body's immune response to allergens. The patents covering the antibody expired in the 2017-2018 timeframe. But to extend its monopoly, Genentech created a thicket of later-filed, secondary patents that includes *US959*, the patent at issue here, which claims a method of treating food allergies in pediatric patients. Long before the earliest possible filing date of *US959*, however, scientists had established that omalizumab was effective at blocking the function of IgE and thus reducing or preventing the body from mounting an acute response to allergens. Because of this efficacy, omalizumab had been approved for the treatment of asthma and nasal polyps, two IgE-mediated diseases, for both adults

and children. Omalizumab had also been studied for the treatment of food allergies in adults and children and proven to be effective.

The challenged claims are directed to a method for treating food allergies in pediatric patients with omalizumab, in which the dose and dosing schedule for a particular child are determined by a simple formula that factors in the child's body weight and serum concentration of IgE antibody prior to treatment.

This method is anticipated by, or obvious over, PO's own prior-art disclosures and other third-party studies. The prior-art label for XOLAIR disclosed that it was dosed for the treatment of asthma and nasal polyps according to a formula based on a patient's weight and pre-treatment IgE levels. Indeed, the prescribing information in the label provided a dosing table to make application of that formula very easy for doctors and patients. The table included dosing information for pediatric body weights, to make dosing children more convenient.

Further, for more than a decade before *US959* was filed, practitioners and scientists had evaluated XOLAIR for the treatment of food allergies in adults and children, both as monotherapy and also in combination with oral immunotherapy. The results were overwhelmingly positive. Two such studies, *MacGinnitie* (EX1008) and *Bégin* (EX1009), include dosing tables adapted to pediatric patients weighing as little as 15 kg. These studies, in particular the dosing tables therein, anticipate at least claims 1, 3, 5, 17-18, and 20-24. The *MacGinnitie* and *Bégin*

references disclose Phase 2 and Phase 1 studies of omalizumab, respectively, and both studies included dosing tables for adults and pediatric patients in which the dose and dosing schedule were determined by body weight and pre-treatment IgE levels. While both references were before the examiner, Genentech did not highlight their materiality to the examiner and the examiner never used them in a rejection. This suggests the examiner either misunderstood the disclosures or did not consider them. Had the examiner properly considered them, the claims would have been rejected as anticipated.

Moreover, all claims would have been obvious to a person of ordinary skill in the art ("POSA"). Recognizing the value in expanding the label for omalizumab to include the treatment of food allergies in both adults and children, Genentech initiated the OUtMATCH study to support approval of XOLAIR for this indication. The OUtMATCH study evaluated omalizumab as a monotherapy and also in combination with oral immunotherapy, and employed a dosing table adapted for both adults and children. Indeed, ameliorating food allergies in children was one of the most promising markets for this label expansion. In fact, "on the basis of data from seven clinical studies over the last decade assessing the efficacy and safety of [omalizumab] against a range of food allergens including peanut, milk, egg and others," Genentech obtained a breakthrough designation for

OUtMATCH. Both the OUtMATCH study protocol and its breakthrough designation are prior art.

Version 26 of the OUtMATCH protocol (*OUtMATCH-V26*) renders obvious all of the challenged claims, in view of what was already known about omalizumab. It teaches the claimed patient population, uses, dosing regimen and calculation of dose and dosing schedule based on weight and pretreatment serum IgE levels.

While *OUtMATCH-V26* did not explicitly disclose the formula used to calculate dose based on weight and IgE levels, a POSA would have understood that *OUtMATCH-V26* applied the claimed formula, which had already been approved for omalizumab and employed in the earlier food allergy studies with omalizumab. Regardless, a POSA seeking to follow the method taught in *OUtMATCH-V26* would have been motivated to apply that formula, since it was used with, and approved for, XOLAIR for many years.

The challenged claims issued only because Genentech did not call the examiner's attention to *OUtMATCH-V26* . Had Genentech done so, the examiner would not have erroneously concluded that the challenged claims were allowable because they disclosed a **new** "relationship" between the mass of a patient, the dose/frequency, and IgE levels. That relationship was disclosed in the prior art,

including *OUtMATCH-V26*, which the examiner never relied upon and which Genentech could not have sworn behind.

In light of this invalidating prior art, Petitioner respectfully submits it has demonstrated at least a reasonable likelihood that the claims are unpatentable and requests institution of *inter partes* review.

A. Overview of *US959*

According to *US959*, food allergies affect "approximately 15 million patients in the U.S., including six million children." Food allergies are one of the most common causes of anaphylaxis seen in children, causing both morbidity and mortality. Therapeutic approaches include counselling patients to avoid their food allergens and prescribing an antihistamine or epinephrine auto-injectors to treat acute allergic food reactions such as anaphylaxis. There is also an approved oral immunotherapy ("OIT") for peanut allergies. Many patients, however, may be allergic to multiple foods. Given that 40% to 70% of children and adults with peanut allergies are also allergic to other foods, *US959* describes treatment for such multiple food allergies as an "unmet need." EX1001, 1:40-60; EX1002 ¶¶ 39-43.

US959 describes and claims methods for treating food allergies. EX1001, 1:30-33. Example 1 of *US959* describes a Phase 3 clinical study, titled OUtMATCH, studying administration of omalizumab in the treatment of food allergies. *US959* asserts that to successfully finish the study, a new dosing table

had to be designed that addressed patients weighing 10-20 kg with total serum IgE levels up to 1800 IU/ml. According to the disclosure, "doses for these weights and serum IgE levels had not been previously determined because there have been no prior regulatory approvals of omalizumab for patients under 6 years of age." *US959* states that stage 1 of the study demonstrated that omalizumab monotherapy was found to be "surprisingly safe and effective" and that this outcome was "particularly striking in young children (1-5 years of age)" for whom Xolair had not previously been approved. *US959* thus describes the alleged invention as treatment of patients from 1 to 5 years old for whom Xolair had not previously been approved. EX1001, 2:43-65; EX1002 ¶44.

Example 1 of *US599* describes the OUtMATCH 3-stage Phase III clinical trial that tested the use of omalizumab for treating patients that are allergic to one or more foods. The study was open to patients from 1 to 55 who are allergic to peanuts and two other foods, such as milk, eggs, wheat, cashew, hazelnut, and walnut. Omalizumab was dosed according to a dosing Table. EX1001, 32:34-44:16, Example 1, FIG 2; EX1002 ¶¶45-47.

The first 60 patients who completed Stage 1 were then selected for the Open Label Extension (OLE), in which they received 24-28 weeks of omalizumab. EX1001, 33:40-46. After those 24-28 weeks, each participant completed a double-blinded, placebo-controlled, food challenge ("DBPCFC") consisting of placebo

and each of their three specific food allergens to a cumulative dose of 8044 mg protein of each food. *Id*. According to *US959*:

> The study met the primary endpoint and achieved statistical significance on the proportion of participants who could consume a single dose of >600 mg of peanut protein without dose-limiting symptoms during the DBPCFC at the end of Stage 1. In the omalizumab-treated group, 68.2% of participants passed the DBPCFC compared to 5.5% in placebo (A: 62.7%, OR: 37.14, p<0.00001).

Id., 40:1-7; EX1002 ¶48.

US959 has 29 claims, four of which are independent. EX1002 ¶49. Claim 1 is representative and is reproduced below:

> 1. A method of treating a human subject having an allergy to a food allergen, the method comprising:
>
> administering to the subject by subcutaneous injection a pharmaceutical composition comprising a dose of omalizumab,
>
> wherein the pharmaceutical composition is administered once about every two weeks and the dose of omalizumab is from 150 mg to 225 mg, or the pharmaceutical composition is administered once about every four weeks and the dose of omalizumab is from 75 mg to 150 mg, and

wherein body weight of the subject is equal to or greater than 10 kg and less than or equal to 15 kg, and total serum IgE level of the subject is equal to or greater than 30 IU/ml and less than or equal to 1850 IU/ml.

B. Prosecution History

US959 issued on July 9, 2024, listing Ryan Patrick Owen, Ahmar Iqbal, and Robert A. Wood as inventors. The underlying application (18/486,053, "*App053*") was filed on October 12, 2023, claiming benefit through a PCT application to provisional application 63/512,051 filed on July 5, 2023. EX1001, 1; EX1002 ¶¶50-51.

App053 was filed listing only a single inventor—Ryan Patrick Owen. EX1004, 101. The examiner, in the first office action on the merits, rejected the claims as anticipated by *Wood* (EX1026). EX1004, 105. *Wood* was cited for disclosing the OUtMATCH clinical trial, in which omalizumab was administered subcutaneously according to Supplemental Figure 1, wherein the dosing was based on the patient's body weight and baseline serum IgE. *Id.*, 105-106. The claims were also rejected as anticipated by *CoFAR* (EX1033), which was cited for its discussion of the OUtMATCH clinical trial. *Id.*, 106-108. The examiner additionally rejected the claims for non-statutory double patenting over the

10,034,940 and 8,961,964 patents, as combined with *Wood* and/or *CoFAR*. *Id.*, 109-116.

In response, PO filed a request for Correction of Inventorship, adding Ahmar Iqbal and Robert Wood as inventors. EX1004, 133-137. PO provided the declaration of Dr. Iqbal, in which Dr. Iqbal testified that to the extent that *Wood* and *CoFAR* described the claimed subject matter, those publications described the work of the inventors. *Id.*, 122-123. PO then argued for withdrawal of the anticipation and double patenting rejections based on Dr. Iqbal's declaration without presenting arguments as to the merits of the rejections. *Id.*, 151-154. The examiner stated in the Notice of Allowance that because the *Wood* and *CoFAR* references are not work done by another and fall within the statutory grace period, they are not prior art. *Id.*, 173-175. The examiner also explained that although the use of omalizumab for treating food allergies was known, the claimed dosing formula based on body mass and serum IgE levels was not:

> [T]he instant claims recite a relationship between the mass of omalizumab administered to the patient, the body mass of the patient, the disease severity as measured by total serum IgE, and the time interval between administrations that was not disclosed in the prior art, nor do the instant recited limitations appear to be obvious variations of prior art dosing protocols. Indeed, the instant recited

patient masses are smaller than those found in dosing charts such as those of the FDA prescribing label for XOLAIR (aka omalizumab, see reference 43 on the 4/30/24 IDS) and thus data on the pediatric patients encompassed by the claimed methods (which even though not recited as being "pediatric," humans of the recited body masses realistically can only be young children) was not present in the prior art.

Id., 175-176; EX1002 ¶52.

C. Scope and Content of the Prior Art

1. Background

a. Food Allergies in Children

As of 2018, food allergies were the main etiology of anaphylaxis in children, which occurred in 10% of food allergic children. EX1006, 286; EX1029, 1901. IgE-mediated forms of food allergy impact 1-10% of infants and pre-school aged children. EX1002 ¶61 (citing EX1030, 1007). As of 2021, food allergies affected about 6 million U.S. children, with a steadily increasing incidence of such allergies. EX1002 ¶¶54-55, 219 (citing EX1005, 5; EX1006, 286; EX1035, 2, EX1041, 65; *see also* EX1021; EX1042). In fact, up to 8% of the pediatric population suffers from food allergies, and of that population, approximately 30% have allergies to multiple foods ("multifood" allergies). EX1009, 1.

Children with multifood allergies experience a greater decrease in the quality of life, are more likely to suffer from dietary deficiencies, and are less likely to outgrow the allergies. EX1009, 1; EX1002 ¶56. As of 2021, the standard of care for food allergy was allergen avoidance, but elimination diets are difficult and frustrating, especially for young children, and accidental exposures were frequent. EX1002 ¶219 (citing EX1006, 286). Young children therefore faced constant risk of accidentally ingesting a food allergen (a frequent occurrence) and having a severe allergic reactions, such as near-fatal or fatal anaphylaxis. EX1018, 16; EX1022, 2; EX1006, 286. Food allergies also placed heavy burdens on families, such as time lost from work and an estimated 200,000 emergency room visits a year, costing billions of dollars a year. EX1009, 1; EX1005, 5; EX1011, 1; EX1002 ¶¶57-58. Reducing the risk of severe allergic reactions reduces the stress of the patient and their families. EX1018, 22; EX1002 ¶¶59-60.

b. Desensitization

Food allergies, including multifood allergies, were often treated by excluding the offending food from the diet and equipping patients with an adrenaline auto-injector. EX1018, 15 (Abstract); EX1036, 258; EX1002 ¶55. Exclusion diets, however, often affected quality of life. EX1018, 15 (Abstract). Moreover, strict food avoidance is especially difficult in children who may not understand food allergy or be able to monitor their own food consumption.

Accidental exposure is common and can be fatal. Food labeling can also be confusing, as labels may not list an allergen such as peanuts, instead stating: "may contain peanuts/nuts" or "processed in a facility that also processes peanuts/nuts." In fact, peanut protein has been found in up 10% of packaged goods with such labeling. EX1023, 76; EX1002 ¶¶104-107.

One method that was used to treat food allergies is oral immunotherapy ("OIT"). EX1008, 874. With OIT, patients are subject to increased amounts of allergen, which can give a majority of subjects tolerance to sufficient doses of the offending food to prevent reaction upon accidental exposure. *Id.* OIT has achieved successful desensitization for a number of foods, including cow's milk, eggs, and peanuts. *Id.* Approximately 20% of subjects undergoing OIT, however, have a severe reaction to the food allergen that requires epinephrine injection, while another 10-20% of patients are refractory to OIT. *Id.*; EX1002 ¶¶62, 185

Accordingly, while desensitization and OIT have been used to treat food allergies, there is a need for additional therapies, especially in children, those refractory to OIT, and those with multifood allergies. Given that one of the critical mediators in food allergy is human immunoglobulin E (IgE), IgE is a target for such therapeutic intervention. EX1037, 4; EX1002 ¶¶63, 72, 94-97.

c. Omalizumab

Omalizumab, trade name XOLAIR, is a recombinant, humanized IgG1 antibody that selectively binds to IgE, which is a key mediator of the body's immune response to allergens. EX1022, 2. Omalizumab inhibits allergic reactions by binding to the constant region of IgE, which causes the body to reduce circulating IgE antibodies and induces a generalized dampening of type 1 allergic immunity. EX1006, 287; EX1028, 72. In this way, IgE is prevented from attaching to specialized immune cells called mast cells and basophils, thus blocking their activation and release of cytokines that are key mediators of an allergic response. EX1006, 287; EX1028, 72; EX1002 ¶¶64-69.

The mode of action of Omalizumab is demonstrated in the Figure below (reproduced from EX1038, 102):

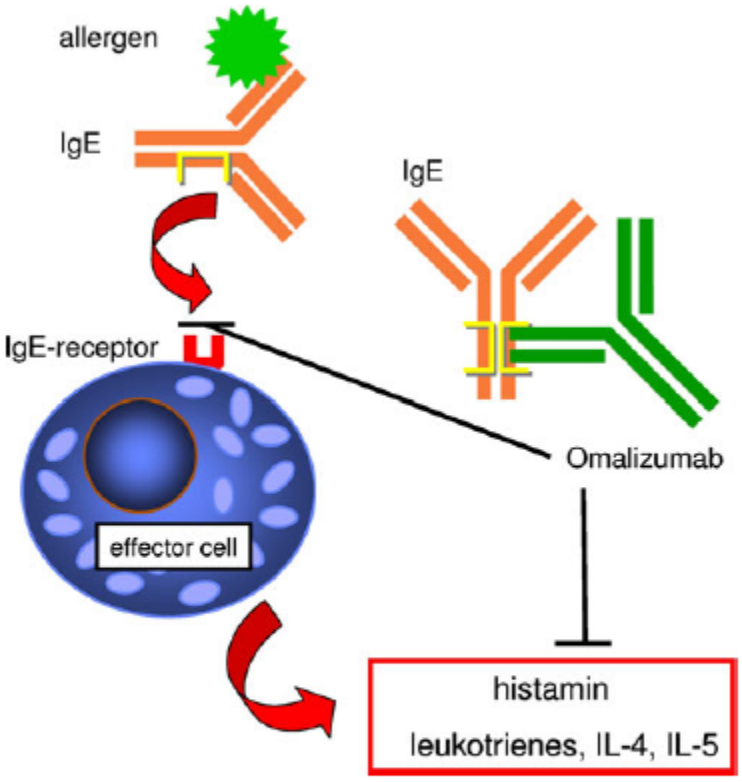

Fig. 1 Mode of action of omalizumab. Omalizumab decreases the levels of circulating IgE regardless of allergen specificity by binding to the constant region of the circulating IgE molecule, which prevents free IgE from interacting with the high- and low-affinity IgE receptors (FcεRI and FcεRII) on effector cells. IL—interleukin

EX1002 ¶¶64-66.

About 20 years before *US959* was filed, omalizumab was approved for treating moderate to severe asthma in adults and adolescents (12 years of age and above) (EX1050), and was later approved for pediatric patients (6 years of age and older) (EX1051). And as of 2021, the clinical efficacy and safety of omalizumab had been explored, with promising results, for treating the following diseases in which IgE plays a role: allergic rhinitis, food and drug allergy, anaphylaxis, keratoconjunctivitis, urticaria, angioedema, allergic bronchopulmonary

aspergillosis, atopic dermatitis, non-allergic asthma, Churg-Strauss syndrome, nasal polyposis, chronic rhinosinusitis, eosinophilic otitis media, bullous pemphigoid, contact dermatitis, and mastocytosis. EX1043, 1-2; EX1044, Abstract; EX1045, Abstract; EX1002 ¶¶69-71, 73, 84.

For asthma and nasal polyps, the omalizumab dosage amount/frequency were based on the total serum IgE (IU/ml) and body weight (kg) before administering omalizumab according to dosing tables. The asthma dosing table for pediatric patients from the July 2021 prescribing information for XOLAIR (*PI2021*, EX1007) is reproduced below. EX1002 ¶140.

Table 2. Subcutaneous XOLAIR Doses Every 2 or 4 Weeks* for Pediatric Patients with Asthma Who Begin XOLAIR Between the Ages of 6 to <12 Years

Pre-treatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight									
		20-25 kg	>25-30 kg	>30-40 kg	>40-50 kg	>50-60 kg	>60-70 kg	>70-80 kg	>80-90 kg	>90-125 kg	>125-150 kg
		Dose (mg)									
30-100	Every 4 weeks	75	75	75	150	150	150	150	150	300	300
>100-200		150	150	150	300	300	300	300	300	225	300
>200-300		150	150	225	300	300	225	225	225	300	375
>300-400		225	225	300	225	225	225	300	300		
>400-500		225	300	225	225	300	300	375	375		
>500-600		300	300	225	300	300	375				
>600-700		300	225	225	300	375					
>700-800	Every 2 weeks	225	225	300	375						
>800-900		225	225	300	375						
>900-1000		225	300	375							
>1000-1100		225	300	375							
>1100-1200		300	300								
>1200-1300		300	375								

Insufficient Data to Recommend a Dose

*Dosing frequency:

- Subcutaneous doses to be administered every 4 weeks
- Subcutaneous doses to be administered every 2 weeks

EX1007, 5; *see also* EX1028, 68. Omalizumab was commercially available in the following presentations: (1) a pre-filled syringe for subcutaneous use containing 75 mg/0.5 mL or 150 mg/mL, and (2) a 150 mg lyophilized powder in a single-dose vial for reconstitution. EX1007, 1. Thus, as evident from the above tables, each dose given to patients was 75 mg, 150 mg, or a multiple thereof. EX1002 ¶¶75, 140-141, 234, 236. In light of the above, *PI2021* states that the recommended dosing for patients with asthma was 75 to 375 mg every two to four weeks based on pretreatment weight and IgE levels. EX1007, 4.

The dosing table was developed based on an algorithm that accounted for both the body mass and baseline plasma concentration of IgE of the individual patient being treated: a patient would receive "at least 0.016 mg of omalizumab per kg of body weight per international unit of baseline IgE per mL per 4 weeks, to reduce the mean free IgE for patients to approximately 25 ng/mL or lower, with most patients achieving free IgE <50 ng/mL." EX1027, 2; *see also id.*, 1 ("An omalizumab dosing table, in which a patient's dosing regimen of omalizumab is determined by a combination of their pre-treatment IgE and body weight, was developed to ensure consistency of free IgE reduction."). *Zhu* found that the pharmacokinetics of omalizumab and its effects on IgE were consistent between asthma and CRSwNP, and explains that the dosing tables for polyps/CRSwNP were therefore based on the same algorithm. *Id.*, 2, 10; EX1002 ¶¶76, 89-90.

Lowe concluded, based on modeling, simulations, and pooled safety data, that two week versus four week dosing does not impact the safety or efficacy of omalizumab. *See* EX1052, 76; EX1002 ¶80.

The prior art, including *PI2021*, also disclosed the use of this algorithm to generate the appropriate dose for an individual patient. With respect to FDA approved prior art uses, for example, *Sandström* teaches that a dose of approximately 0.016 mg/kg per IU/ml of IgE according to bodyweight and baseline IgE can reduce free IgE by 89-99% in patients with allergic asthma and allergic rhinitis. EX1046, 50-51; EX1002 ¶77. Consistent with this, *PI2021* describes clinical trials for asthma in which "[p]atients were treated according to a dosing table to administer at least 0.016 mg/kg/IU (IgE/mL) of [omalizumab] … over each 4-week period." EX1007, 24.

Many other prior art references reiterate the same dosing algorithm for investigational new uses of omalizumab, like treatment of food allergies and treatment of patients as young as 2-3 years old. *See* EX1027, 2 (dosing for CRSwNP and allergic asthma based on administering at least 0.016 mg/kg of body weight/IU); EX1028, 68 (same dosing algorithm); EX1017, 6 (same dosing algorithm for 2-3 year olds at high-risk for developing asthma); EX1031, 1309 (same dosing algorithm); EX1006, 289-290 (majority of studies of omalizumab monotherapy for treating food allergy set dosage/frequency based on total serum

IgE level/subject weight "according to asthma and nasal polyps indication"); EX1002 ¶¶81, 109-111.

Omalizumab had a proven safety profile in adults, adolescents, and children. EX1046, 56-57. By April 2007, approximately 68,000 moderate-to-severe allergic asthma patients had been treated with omalizumab. *Id.*, 57.

Asthma "is the most common noncommunicable disease in children worldwide," and at least 90% of these children have underlying allergies confirmed by IgE mediated aeroallergen sensitivity. EX1047, 1; EX1002 ¶86. Atopy, a genetic predisposition to the production of IgE, is the underlying cause of most cases of asthma. EX1046, 49; EX1002 ¶87.

Before the earliest possible effective filing date of *US959*, omalizumab had been used in patients with asthma, or a high probability of getting asthma, including children as young as 2. For example, *Phipatanakul* performed a double-blind, placebo-controlled trial of omalizumab in 250 children ranging in age from 24 to 47 months at high risk for developing asthma, to prevent the development and reduce the severity of asthma. According to the authors, "[i]t took over a decade of working with the Food and Drug Administration and amassing real world omalizumab safety data for nearly two decades before an Investigational New Drug (IND) was granted down to age 2 years." EX1017, 19. Omalizumab was administered to patients subcutaneously every 4 weeks ensuring at least 0.016

mg/kg/IU total IgE (measured at screening) in 75 mg increments utilizing pre-filled 75 mg and 150 mg syringes (PFS) with a maximum dose of 25 mg/kg, and epinephrine auto injectors were provided to the families of subjects, including subjects weighing <15 kg. According to the authors, using the dosing algorithm "allow[s] the widest range of children to be covered." EX1017, Abstract, 3, 6, 19; EX1002 ¶82-83.

Since patients with allergic asthma often have other diseases (co-morbidities) that are also are IgE-mediated, scientists began studying whether omalizumab could be effective at treating these related diseases as well. EX1045, Abstract, 1418-1419; EX1006, 287; EX1028, 72; EX1002 ¶¶85-88. *Fiocchi 2019* analyzed the effects of omalizumab on food allergies in children administered omalizumab for asthma. *Fiocchi 2019* notes that OIT in children with multiple food allergies is problematic, and thus additional therapies are needed. Given that anti-IgE therapies had reduced the likelihood of anaphylaxis in patients with peanut allergies who had accidental exposure, the researchers hypothesized that children with allergies treated with omalizumab would have increased tolerance to foods to which they are allergic. The authors concluded that omalizumab was well tolerated, with children reaching full tolerance 70.6% of the foods tested. EX1029, Abstract, 1902, 1905-6; EX1002 ¶¶91-92, 115.

Omalizumab has also been used to specifically treat patients with food allergies. EX1002 ¶93. *Takahashi* studied omalizumab use in subjects 6-14 years of age with high-risk allergies to cow's milk. While the study was initially designed for 50 subjects, the study was prematurely discontinued after only 16 subjects completed the study "due to overwhelming superiority of [omalizumab] combined with microwave heated OIT over [cow's milk] avoidance." EX1039, Abstract. All of the subjects had high-risk of life-threatening anaphylaxis from cow's milk and all achieved desensitization. Omalizumab doses were provided based on a formula provided by Genentech. EX1039, Abstract, 5, 7-8; EX1002 ¶101.

Martorell-Calatayud also looked at omalizumab assisted OIT in 3 to 13 year old patients allergic to cow's milk and eggs, who could not tolerate conventional OIT; omalizumab was dosed according to the package insert. Desensitization began after the start of omalizumab treatment. During the 18 week induction phase, only 28% (4) of the patients experienced mild allergic reactions. *Id.* By the end of the induction phase, all patients achieved complete desensitization. The authors found that "[a]ssociation of omalizumab allows safe and effective desensitization treatment in patients who have been refractory to it," concluding that "[s]afer OIT would allow OIT to become widely available to patients with

food allergy and associations with omalizumab could be the key to opening that door." EX1040, 1-3; EX1002 ¶100.

In addition, *MacGinnitie* studied omalizumab as an add-on to desensitization of peanut allergy subjects. After 12 weeks of treatment, the median dose of peanut protein tolerated by omalizumab treated patients was 250 mg compared to 22.5 mg for those on placebo. After continued treatment, 22 omalizumab subjects met a challenge of 4000 mg, compared to only one placebo arm subject, and, in a majority of subjects, desensitization was sustained even after discontinuing omalizumab treatment. The authors noted that while omalizumab is expensive and requires repeated injections, "the benefits of omalizumab-enabled OIT might outweigh these downsides." EX1008, Abstract, 875-877, 880; EX1002 ¶¶99, 144-149.

Andorf 2018 conducted a pilot study of the safety and efficacy of treating multifood allergies with omalizumab. It had previously been shown that OIT combined with omalizumab could rapidly achieve desensitization in subjects allergic to single foods. Omalizumab or placebo was administered to 48 participants, aged 4-15, along with multifood OIT to 2-5 foods chosen from cashew, walnut, hazelnut, almond, sesame, cow's milk, hen's egg, peanut, soy, and wheat. The foods used for OIT were those to which the subject had previously experienced a significant allergic reaction. Participants received omalizumab or

placebo subcutaneously for 16 weeks, with multifood OIT starting at 8 weeks. Omalizumab was dosed according to the manufacturer's instructions in the product insert. The researchers concluded that "patients with multifood allergies can be safely and effectively desensitized to their offending foods with a combination of multifood oral immunotherapy with omalizumab treatment." EX1022, 14. The omalizumab arm also provided increased safety, such as reductions in gastrointestinal and respiratory symptoms, and shorter times to reach an OIT maintenance dose. EX1022, Abstract, 2, 5-8, 14; EX1002 ¶102.

In 2019, *Andorf 2019* reported that "desensitization with omalizumab-facilitated multifood OIT (up to 5 allergens) can be achieved in the majority of participants at multiple clinical sites within 30 weeks," demonstrating that "omalizumab-facilitated multifood-OIT can be performed in multiple centers with a standardization protocol in a safe manner, with a high rate of completion." EX1048, 28. *Andorf 2019* concluded that sustained desensitization was achievable and improved quality of life. *Id.*; EX1002 ¶103.

In 2014, *Bégin* reported that administering omalizumab according to the product insert to subjects 4 years of age or older with multifood allergies "demonstrate[d] that rush OIT to multiple foods with 16 weeks of treatment with omalizumab could allow for a fast desensitization in subjects with multiple food allergies." EX1009, Abstract, 2-3. *Crespo* similarly used omalizumab to treat

children from ages 4.5 and 8.25 years diagnosed with multifood allergies who also presented with anaphylaxis. After omalizumab treatment, the subjects did not show reactions to most of the foods to which they previously had anaphylactic reactions, thereby allowing subjects to improve their quality of life, expand their diets, and avoid anaphylaxis due to inadvertent intake of food allergens. EX1018, Abstract; EX1002 ¶116.

The prior art also taught the use of omalizumab as a monotherapy for food allergies. For example, *Arasi* taught that data from early clinical trials demonstrated that omalizumab monotherapy could provide desensitization to one or multiple foods without exposing the subject to the allergen. *Arasi*, in Table 1, summarizes findings from the most relevant studies of omalizumab monotherapy. In one study where omalizumab was used to treat severe atopic asthma, 15 of the 115 subjects were allergic to at least two foods. After treatment for four months, all 15 of these patients demonstrated an increase in their eliciting threshold for the food allergen, and 9 could tolerate a full serving of the offending food. EX1006, 286-289; EX1002 ¶136; *see also* EX1020.

As yet another example, in *Peloche*, ten patients over age 6 received 16 weeks of omalizumab treatment, after which they were challenged with a single blinded food. None of the study patients had a single adverse reaction. Eight patients underwent the blind food challenge, with four demonstrating complete

tolerance, and all patients exceeded their baseline threshold dose. The authors concluded that "[a]nti-IgE therapy has proven an effective and safe measure in the treatment of the persistent and severe allergy to milk and egg, whether used as monotherapy or as an adjuvant measure to the process of desensitization to food, making it safer and faster procedure." EX1024; EX1025; EX1002 ¶108.

Additionally, in August 2018, FDA granted Breakthrough Therapy Designation ("BTD") for omalizumab for the prevention of severe allergic reaction to accidental exposure to one or more foods in people with allergies to one or more foods. EX1011. A drug may receive BTD if it is intended to treat a serious or life-threatening disease and preliminary clinical evidence indicates that it provides a substantial improvement over existing therapies. EX1012, 1. Omalizumab's BTD was a result of "data from seven clinical studies over the last decade assessing the efficacy and safety of [omalizumab] against a range of food allergens including peanut, milk, egg and others." EX1011, 1; EX1002 ¶¶118-119.

Omalizumab's BTD led to Genentech, Novartis, and the National Institute of Allergy and Infectious Diseases ("NAIAD") launching the Omalizumab as Monotherapy and as Adjunct Therapy to Multi-Allergen Oral Immunotherapy in Food Allergic Children and Adults ("OUtMATCH") study in March 2019. *OUtMATCH-V26* included participants 1-55 years of age allergic to peanut and at least two other foods, wherein: (a) patients received omalizumab by subcutaneous

injection every two or four weeks; (b) the dosing amounts and interval were determined by serum total IgE level and body weight (measured before the start of treatment) per a study drug dosing table; and (c) omalizumab was supplied in 75 mg and 150 mg pre-filled syringes. EX1005, 5, 6; EX1002 ¶¶120-122.

2. Key Prior Art

a. Omalizumab as Monotherapy and as Adjunct therapy to Multi-Allergen OIT in Food Allergic Participants, Version 26 (EX1005; *OUtMATCH-V26*)

OUtMATCH-V26 published May 2, 2022, more than one year before *US959*'s earliest possible priority date of July 5, 2023, and is therefore prior art . Post-AIA 35 U.S.C. §102(a)(1); IPR2022-00578, Paper 78 at 25-28 (finding that a clinical trial protocol published on ClinicalTrials.gov is prior art). *OUtMATCH-V26* describes a multi-center, randomized, double-blind, placebo-controlled Phase 3 clinical trial with participants aged 1-55 years old who are allergic to peanut and at least two other foods. Stage 1 of the study investigated whether "omalizumab [monotherapy] stops or decreases allergic reactions to peanut and other common food allergens after taking it for a length of time." EX1005, 5. *OUtMATCH-V26* discloses that omalizumab will be administered "by subcutaneous injection either every 2 weeks or every 4 weeks for 16 to 20 weeks" and that "[t]he dose administered and the dosing interval are determined by serum total IgE level and body weight (measured before the start of treatment) per the study drug dosing

table." *Id.*, 6. *OUtMATCH-V26* further states that "[o]malizumab will be supplied in pre-filled syringes (PFS)" as "75 mg and 150 mg dosage forms." *Id.*, 6, 7; EX1002 ¶¶124-130.

b. *Arasi* (EX1006)

Arasi, titled "Omalizumab as a monotherapy for food allergy," published in 2021, more than one year before *US959*'s earliest possible priority date of July 5, 2023, and is therefore prior art. Post-AIA 35 U.S.C. §102(a)(1). EX1002 ¶132. *Arasi* describes a need for therapies for patients with food allergies, stating that "the most promising therapeutic options are oral immunotherapy (OIT) and biologicals; among the latter, Omalizumab is the most used either combined with OIT or as a monotherapy." EX1006, 286 (internal citations omitted). *Arasi* explains that omalizumab is an anti-IgE humanized monoclonal antibody that "by binding to the IgE constant Cε3 region of free circulating IgE, prevents the latter from binding to the high-affinity FcεR1 receptors on effector cells (primarily basophils and mast cells), interfering with degranulation and release of pro-inflammatory mediators." *Id.*; EX1002 ¶133.

Arasi notes the following key points:

- "The property of Omalizumab to induce [non]-allergen-specific effects on allergic immune responses makes this biological treatment

a potentially attractive candidate for several IgE-mediated diseases including food allergy." *Id.*, 287; EX1002 ¶134.

- "The current data from early stage clinical trials show that Omalizumab may be effective by itself in providing desensitization to one or several foods without requiring allergen exposure as in oral immunotherapy." *Id.*; EX1002 ¶¶117, 135.

Arasi summarizes the results of three studies (EX1031, EX1032, and EX1029) that evaluated the use of monotherapy omalizumab in food allergy and reported that patients experienced large, statistically significant increases in tolerated doses of food allergens compared to baseline. EX1006, 288 (summarizing "main findings" of EX1031, EX1032 (about 80-fold increase in tolerated dose), and of EX1029 (results represented "statistically significant improvement for egg, milk, baked milk, and wheat"); EX1002 ¶¶109-112, 136. With respect to dosing, *Arasi* states: "The majority of studies report on the administration of [omalizumab] with a dosage and a frequency (every 2 or 4 weeks) set based on the total serum IgE level and the weight of the individual patient, according to asthma and nasal polyps indication" and that "Omalizumab has been reported to be used also in subjects with total IgE up to 2,000 IU/mL without any specific safety concern." EX1006, 289-290 (citing EX1008); EX1002 ¶136-138.

c. *MacGinnitie* (EX1008)

MacGinnitie, titled "Omalizumab facilitates rapid oral desensitization for peanut allergy," published in 2016, more than one year before *US959*'s earliest possible priority date of July 5, 2023, and is therefore prior art. Post-AIA 35 U.S.C. §102(a)(1). *MacGinnitie* discloses the results of a randomized, double-blind, placebo-controlled phase II clinical trial of omalizumab as an add-on to peanut allergy desensitization therapy in which omalizumab was administered once every two or four weeks to subjects weighing as little as 15-20 kg with baseline IgE of 30-2000 IU/mL. EX1008, 875-880, 881e.3; EX1002 ¶¶99, 143-149.

d. *Bégin* (EX1009)

Bégin, titled "Phase 1 results of safety and tolerability in a rush oral immunotherapy protocol to multiple foods using Omalizumab," published in 2014, more than one year before *US959*'s earliest possible priority date of July 5, 2023, and is therefore prior art. Post-AIA 35 U.S.C. §102(a)(1). *Bégin* discloses the results of phase 1 of a clinical trial of omalizumab in which omalizumab was administered once every two weeks or every four weeks to subjects weighing as little as 15-20 kg with baseline IgE of 30-2000 IU/mL. EX1009, 4-8, 10.s2, Table E2; EX1002 ¶¶98, 150-157.

e. *PI2021* (EX1007)

PI2021, the July 2021 prescribing information for XOLAIR, published in July 2021, more than one year before *US959*'s earliest possible priority date of July 5, 2023, and is therefore prior art. Post-AIA 35 U.S.C. §102(a)(1).

PI2021 discloses omalizumab dosing tables, based on weight and baseline total serum IgE, for the treatment of asthma and polyps, with asthma subjects weighing as little as 20 kg and having baseline IgE of 30-1300 IU/mL. *PI2021* states that "[t]he recommended dosage for treatment of asthma is XOLAIR 75 mg to 375 mg by subcutaneous injection every 2 or 4 weeks based on serum total IgE level (IU/mL) measured before the start of treatment and by body weight (kg)." EX1007, 4. In the asthma clinical trial, "[p]atients were treated according to a dosing table to administer at least 0.016 mg/kg/IU (IgE/mL) of [omalizumab] … over each 4-week period" and "[t]he maximum XOLAIR dose per 4 weeks was 750 mg." *Id.*, 24. *PI2021* also states that omalizumab is supplied as 75 mg and 150 mg prefilled syringes. *Id.*, 3-5, 20, 24, 34; EX1002 ¶¶139-142.

3. Level of Ordinary Skill in the Art

A POSA would have been a medical doctor and/or clinical researcher with a Ph.D. and significant experience treating and/or researching food and other allergies. The POSA would have collaborated with others, including scientists

skilled in related fields typically employed in pharmaceutical development, such as pharmacokineticists and formulators. EX1002 ¶¶36-38.

II. GROUNDS FOR STANDING (37 C.F.R. §42.104(A))

Petitioner certifies that *US959* is available for IPR and that Petitioner is not barred or estopped from bringing this petition or challenging any claim of *US959* on the grounds identified herein. Petitioner has not filed a civil action challenging the validity of *US959*.

III. MANDATORY NOTICES UNDER 37 C.F.R. §42.8

Pursuant to 37 C.F.R. §§42.8(a)(1) and 42.8(b), the following mandatory notices are provided as part of this Petition.

A. Real-Party-in-Interest (37 C.F.R. §42.8(b)(1))

Amneal Pharmaceuticals, Inc. and Kashiv BioSciences are the real parties in interest.

B. Related Matters (37 C.F.R. §42.8(b)(2))

Petitioner is not aware of any related matters.

C. Lead and Back-Up Counsel and Service Information (37 C.F.R. §42.8(b)(3), (4))

Lead counsel is Lora M. Green (Reg. No. 43,541). Back-up counsel are Robert Cerwinski (to be admitted *pro hac vice*), Keith A. Zullow (Reg. No. 37,975), Michael Cottler (Reg. No. 79,455), and Yahn-Lin (Franklin) Chu (Reg. No. 75,946).

Petitioner hereby consents to electronic service. Please direct all correspondence to lead and back-up counsel at the contact information below. A power of attorney accompanies this petition.

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D. Payment of Fees Under 37 C.F.R. §42.15(a) and §42.103

The required fees are submitted herewith. If any additional fees are due at any time during this proceeding, the Office is authorized to charge such fees to Deposit Account No. 604962.

IV. OVERVIEW OF CHALLENGE AND PRECISE RELIEF REQUESTED

A. Challenged Claims and Relief Requested

Petitioner requests institution of IPR against claims 1-29 of *US959* and cancellation of these claims as unpatentable.

B. Statutory Grounds of Challenge

Each of the following prior art references and/or combinations of references renders the challenged claims unpatentable:

Ground	Claims	35 U.S.C.	References
1	1, 3, 5, 17-18, 22-24	§102	*MacGinnitie* (EX1008)
2	1, 3, 5, 17-18, 22-24	§103	*MacGinnitie*
3	1, 3, 5, 17-18, 20-23	§102	*Bégin* (EX1009)
4	1, 3, 5, 17-18, 20-23	§103	*Bégin*
5	1-29	§103	*OUtMATCH-V26* (EX1005), *PI2021* (EX1007), and *Arasi* (EX1006)

Petitioner's full statement of the reasons for the relief requested is set forth in greater detail below, as supported by the declaration of Dr. Asif Rafi (EX1002). Dr. Rafi has extensive experience in treating allergies, including food allergies, and was lead author on one of the earliest articles on the use of omalizumab for the treatment of food allergies. EX1002 ¶¶4-11; EX1003.

V. CLAIM CONSTRUCTION

Claim terms should be given their ordinary and customary meaning consistent with the specification, as a POSA would have understood them. 37 C.F.R. § 42.100(b); *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (*en banc*). Accordingly, the terms of the challenged claims should be given

their plain and ordinary meaning. Two claim terms are specifically discussed below. Regardless of the claim construction adopted, the challenged claims are unpatentable over the prior art.

A. The Claim Term "Or" Denotes Alternatives

Claims 1, 2, 5, 10-12, 17, and 25 include alternative dosing regimens separated by the word "or." For example, claim 1 states: "wherein the pharmaceutical composition is administered once about every two weeks and the dose of omalizumab is from 150 mg to 225 mg, ***or*** the pharmaceutical composition is administered once about every four weeks and the dose of omalizumab is from 75 mg to 150 mg" (emphasis added). As used in the *US959* claims, the term "or" should be given its common meaning as a designator of alternatives. EX1002 ¶¶15, 162; *see Kustom Signals, Inc. v. Applied Concepts, Inc.*, 264 F.3d 1326, 1331 (Fed. Cir. 2001). In the claims, it designates alternative dosing regimens for each individual subject based on the subject's weight and total serum IgE level. Nothing in the *US959* specification or file history suggests deviating from the common use of the term "or" as designating alternatives.

B. "A human subject" and "the subject" Encompass a Single Subject

The methods of independent claims 1, 12, 17, and 25 all recite "[a] method of treating a human subject … comprising: administering to the subject" and also include recitations directed to the body weight and IgE of "the subject." A POSA

would have understood that treating "a human subject" by administering omalizumab to "the subject" based on the body weight and IgE of "the subject" encompasses a dosing regimen for treating a single subject that has characteristics falling within the scope of the claim. EX1002 ¶163.

VI. GROUNDS FOR UNPATENTABILITY

A. Ground 1: Claims 1, 3, 5, 17-18, and 22-24 are Anticipated by *MacGinnitie* (EX1008)

MacGinnitie discloses each and every element of claims 1, 3, 5, 17-18, and 22-24. EX1002 ¶¶159-185.

1. Claim 1

Claim 1 is drawn to (a) a method of treating a human subject having an allergy to a food allergen, the method comprising: (b) administering to the subject by subcutaneous injection a pharmaceutical composition comprising a dose of omalizumab, wherein (c) the subject weighs ≥10 kg to ≤15 kg, and (d) has a total serum IgE level of ≥30 IU/ml to ≤1850 IU/ml, and (e) wherein the dose is 150-225 mg every two weeks ***OR*** 75-150 mg every four weeks. *See* Section I.A. Because it uses the term "or", claim 1 recites alternative dosing regimens: (a) 150-225 mg every two weeks; or (b) 75-150 mg every four weeks. Anticipation requires prior art disclosure of only one of the claimed alternatives. Moreover, the claim encompasses the treatment of a single subject. Accordingly, the treatment of a single subject with one of the alternative treatments anticipates the claim.

As explained below, *MacGinnitie* discloses this treatment, along with every other element of claim 1 as arranged in the claim. It therefore anticipates claim 1. *See generally* EX1008; EX1002 ¶¶159-172.

a. Treating a Human With a Food Allergy

To the extent that the preamble is limiting, *MacGinnitie* discloses that it "provides rigorous scientific confirmation that omalizumab can facilitate rapid OIT of high-risk subjects with peanut allergy," and thus discloses using omalizumab to treat a human with a food allergy. EX1008, 877; EX1002 ¶165. *MacGinnitie* meets this treating element.

b. Administration of Omalizumab by Subcutaneous Injection

MacGinnitie discloses that "[s]tudy drug [omalizumab] was administered by means of subcutaneous injection," meeting this subcutaneous injection element. EX1008, 881.e1; EX1002 ¶166.

c. Subject Weight 10-15 kg

MacGinnitie discloses a dosing table that includes administering omalizumab to subjects weighing 15-20 kg, which includes administering omalizumab to a subject weighing 15 kg, meeting this subject weight element. EX1008, 881.e3; EX1002 ¶167. *E.g.*, *Titanium Metals Corp. v. Banner*, 778 F.2d

775, 782 (CAFC 1985) (even if a claim covers only one composition in a composition defined by ranges, the claim is anticipated).

d. Subject Having Total IgE Serum Level of 30 – 1850 IU/ml

MacGinnitie discloses treating subjects with "baseline … total IgE level of 50 IU/L or greater but 2000 IU/L or less" (which a POSA would have understood as IU/ml) and a dosing table that includes administering omalizumab to subjects weighing 15-20 kg with baseline/screening IgE (IU/mL) of 30-2000. EX1008, 881.e1, .e3; EX1002 ¶168. The dosing table includes screening IgE ranges of, for example, 30-100, 101-200, and 701-800 IU/mL, which are entirely encompassed by the claimed range. EX1008, 881.e3. *MacGinnitie* thus meets the IgE level element. EX1002 ¶168.

e. Dose of 150-225 mg Once About Every Two Weeks or 75-150 mg Once About Every Four Weeks

For a 15 kg subject, the *MacGinnitie* dosing table discloses administering 225 mg of omalizumab once every two weeks to, for example, a subject having a screening IgE 701-800 IU/mL, or administering 75 mg once every four weeks to a subject having a screening IgE of 30-100 IU/mL. EX1008, 881.e3. The dosing table also discloses administering 150 mg once every four weeks to a subject

having a screening IgE of 201-300 IU/mL. *Id.* *MacGinnitie* meets this dose amount/frequency element. EX1002 ¶¶169-171.

For all of the above reasons, *MacGinnitie* discloses every element of claim 1, arranged as in the claim, and anticipates claim 1. EX1002 ¶¶159-172.

2. Claims 3 and 5

Claim 3 depends from claim 1 and requires that omalizumab be administered once about every four weeks at a dose of 75 mg when baseline IgE is ≥30 and ≤300 IU/ml, and further requires that the subject's total serum IgE level is determined prior to administering a first dose of omalizumab. Claim 5 depends from claim 1 and includes as one of its dosing alternatives that, for a subject with a body weight of > 12 kg and ≤ 15 kg, the dose of omalizumab is 75 mg once about every four weeks for a subject with a baseline total serum IgE of ≥30 and ≤300 IU/ml and further requires that the subject's total serum IgE level is determined prior to administering a first dose of omalizumab. EX1002 ¶¶173-175.

As explained above, the *MacGinnitie* dosing table states that dosing is "based on body weight and baseline total IgE level," and discloses that for a 15-20 kg subject, which would include a 15 kg subject, a dose of 75 mg of omalizumab should be administered once every four weeks to a subject having a screening/baseline total IgE of 30-100 IU/ml. EX1008, 881.e3; 881.e1; EX1002 ¶176. Furthermore, because administration is based on baseline total IgE,

total serum IgE had to have been measured before dosing. Therefore, *MacGinnitie* meets this requirement. EX1002 ¶¶177-178.

For these reasons and those explained with regard to claim 1 (Section VI.A.1.), *MacGinnitie* discloses all of the elements of claim 3 arranged as in the claim. EX1002 ¶¶158-174. Moreover, administering 75 mg of omalizumab once every four weeks to a subject having a screening IgE of 75, as disclosed in *MacGinnitie*, satisfies the alternative in claim 5 that requires administering, to a subject weighing >12 kg and ≤15 kg, 75 mg once about every four weeks if the total serum IgE level of the subject is ≥30 IU/ml and ≤300 IU/ml. EX1008, 881.e3; EX1002 ¶¶175-177. For these reasons and those explained with regard to claim 1, *MacGinnitie* discloses all of the elements of claim 5 arranged as in the claim. EX1002 ¶¶158-172, 175-178. *MacGinnitie* thus anticipates claims 3 and 5.

3. Claim 17

Claim 17 claims a method of treating a human subject having an allergy to a food allergen, the method comprising, among other things, administering to the subject by subcutaneous injection once about every four weeks a pharmaceutical composition comprising a dose of omalizumab of 75 mg once for a subject with a total serum IgE of ≥30 and ≤300 IU/ml, wherein the total serum IgE level of the subject is determined prior to administration of a first dose of omalizumab. For the same reasons as set forth above with respect to claim 3, *MacGinnitie* discloses all

elements of the above alternative of claim 17, arranged as in the claim, and anticipates claim 17. EX1008, 881.e1, 881.e3; EX1002 ¶¶158-174, 179-181.

4. Claim 18

Claim 18 depends from claim 17 and further requires that the body weight of the subject be determined prior to administration of a first dose of omalizumab. *MacGinnitie* discloses that "dosing was based on weight and IgE level." EX1008, 881.e1. As dosing is based on weight, the weight of the subject had to have been determined before the administration of omalizumab. EX1002 ¶182. Accordingly, *MacGinnitie* meets the added limitation of claim 18. For this reason and those explained with regard to claim 17, *MacGinnitie* anticipates claim 18. EX1002 ¶¶158-174, 179-182.

5. Claims 22-24

Claim 22 depends from claim 17 and further requires that the treating comprises reducing an allergic reaction following exposure of the subject to the food allergen. Claim 23 depends from claim 22 and further requires that "the exposure to the food allergen is accidental." Claim 24 depends from claim 22 and further requires that "the allergic reaction is a moderate to severe allergic reaction." EX1002 ¶183. *MacGinnitie* discloses the following: "The primary end point … was the ability to tolerate a 2000-mg dose of peanut protein 6 weeks after stopping omalizumab or placebo injection. This was achieved in 23 of 29 subjects

randomized to omalizumab (79% of the ITT population) and 23 (85%) of 27 who actually received peanut immunotherapy compared with 1 (12.5%) of 8 receiving placebo ($P < 0.01$ for the ITT population, Table II)." EX1008, 875, 878. Accordingly, *MacGinnitie* meets the added limitations of claim 22. EX1002 ¶¶183-184. Moreover, based on these results, the reduction in allergic reaction would be observed after an accidental exposure, and *MacGinnitie* also meets the added limitations of claim 23. *Id.*

MacGinnitie states that approximately 20% of subjects undergoing OIT experience severe reactions requiring injection of epinephrine. EX1008, 874. *MacGinnitie* found that six of eight placebo-treated subjects had moderate reactions, while only 4 of 28 omalizumab-treated subjects had such reactions. *Id.*, 876. Accordingly, *MacGinnitie* disclosed that omalizumab reduced moderate-to-severe allergic reactions and therefore *MacGinnitie* meets the added limitation of claim 24. EX1002 ¶185.

B. Ground 2: Claims 1, 3, 5, 17-18, and 22-24 are Obvious Over *MacGinnitie* (EX1008)

Ground 1 is incorporated by reference. Section VI.A. To the extent *MacGinnitie* fails to anticipate claims 1, 3, 5, 17-18, and 22-24 by not explicitly exemplifying treatment of a 15 kg patient, it renders those claims obvious. EX1002 ¶186. The *MacGinnitie* dosing table (Table E2) includes omalizumab dosing amounts/frequencies for patients weighing 15-20 kg, which includes 15 kg

patients, and patients with baseline IgE of 30-100, 101-200, and 701-800, all of which are completely within the claimed ranges. EX1008, 881.e3. Based on Table E2, a POSA would have been motivated to treat 15 kg subjects with the following dosing regimens based on their screening/pre-treatment total serum IgE. A POSA would have had a reasonable expectation of success because *MacGinnitie* discloses that omalizumab achieved rapid desensitization against peanut allergy. Accordingly, the following claims reciting the indicated screening IgE, dosage amount, and dosing frequency would have been obvious:

Screening IgE (IU/mL)	**Amount (mg)**	**Frequency**	**Claims Rendered Obvious**
30-100	75	Every 4 weeks	1, 3, 5, 17-18, 22-24
101-300	150	Every 4 weeks	1
701-800	225	Every 2 weeks	1

EX1008, 881.e3, Table E2; EX1002 ¶¶187-189; *see Guardant Health, Inc. v. Univ. of Wash.*, Case No. 2024-1129, 2026 U.S. App. LEXIS 1651, at *11-12 (Fed. Cir. Jan. 23, 2026) ("When the disputed elements of a claim are disclosed in a single embodiment in a single reference, no finding regarding a motivation to combine to arrive at those claimed elements is required.").

For the above reasons, including those in Sections I.C.2.c. and VI.A., *MacGinnitie* would have rendered claims 1, 3, 5, 17-18, and 22-24 obvious to a POSA. EX1002 ¶¶186-190.

C. Ground 3: Claims 1, 3, 5, 17-18, and 20-23 are Anticipated by *Bégin* (EX1009)

Bégin discloses each and every element of claims 1, 3, 5, 17-18, and 20-23.

1. Claim 1

The elements of claim 1 are set forth above. Section VI.A.1. As explained below, *Bégin* meets every element of claim 1 as arranged in the claim and therefore anticipates claim 1. *See generally* EX1009; EX1002 ¶¶191-200.

a. Treating a Human With a Food Allergy

To the extent that the preamble is limiting, *Bégin* discloses using omalizumab and OIT to treat human "[p]articipants with multiple food allergies," and thus discloses using omalizumab to treat a human with a food allergy. EX1009, 1 (and 2, 5, Table E3); EX1002 ¶193. *Bégin* meets this treating element.

b. Administration of Omalizumab by Subcutaneous Injection

Bégin discloses that omalizumab "was prepared and administered according to the product insert" and that "[o]malizumab injections were administered." EX1009, 3. In 2014 (when *Bégin* was published), the only route of administration in the Xolair product insert was subcutaneous injection; EX1002 ¶194; EX1019, 2 ("Administer Xolair 150 to 375 mg by subcutaneous injection every 2 or 4

weeks.") Accordingly, *Bégin* discloses this subcutaneous injection element. EX1002 ¶194.

c. Subject Weight 10-15 kg

Bégin discloses a dosing table that includes administering omalizumab to subjects weighing 15-20 kg, which includes administering omalizumab to a subject weighing 15 kg, meeting this subject weight element. EX1009, Supplemental Table E2; EX1002 ¶195. *E.g.*, *Titanium Metals*, 778 F.2d at 782.

d. Subject Having Total IgE Serum Level of 30–1850 IU/ml

Bégin discloses a dosing table that includes administering omalizumab to subjects weighing 15-20 kg, with screening/baseline total IgE of 30-1500 IU/mL, which range is entirely encompassed by the claimed range. EX1009, Supplemental Table E2. *Bégin* thus meets this IgE level element. EX1002 ¶196.

e. Dose of 150-225 mg Once About Every Two Weeks or 75-150 mg Once About Every Four Weeks

For a 15 kg subject, the *Bégin* dosing table discloses administering 225 mg of omalizumab once every two weeks to, for example, a subject having a screening IgE of 701-800 IU/mL, administering 75 mg once every four weeks to a subject having a screening IgE of 30-100 IU/mL, and administering 150 mg once every four weeks to a subject having a screening IgE of 101-200 IU/mL, meeting this

dose amount/frequency element. EX1009, Supplemental Table E2; EX1002 ¶¶197-199.

For all of the above reasons, *Bégin* discloses every element of claim 1, arranged as in the claim, and therefore anticipates claim 1. EX1002 ¶¶191-200.

2. Claims 3 and 5

The elements of claims 3 and 5 are set forth above in Section VI.A.2. As explained above, for a 15-20 kg subject, which includes a 15 kg subject, the *Bégin* dosing table discloses administering 75 mg of omalizumab once every four weeks to a subject having a screening IgE of 30-100. EX1009, Supplemental Table E2; EX1002 ¶201. Furthermore, because administration is based on the screening serum IgE, IgE had to have been measured before dosing. EX1002 ¶202. *Bégin* thus meets the requirement of determining total serum IgE prior to administration of a first dose of omalizumab. For these reasons and those explained with regard to claim 1 (Section VI.C.1.), *Bégin* discloses all of the elements of claim 3 arranged as in the claim. Moreover, administering 75 mg of omalizumab once every four weeks to a subject weighing 15 kg and having a screening IgE of 30-100, as disclosed in *Bégin*, satisfies the alternative in claim 5 that requires administering, to a subject weighing >12 kg and ≤15 kg, 75 mg once about every four weeks if the total serum IgE level of the subject is ≥30 IU/ml and ≤300 IU/ml. EX1009, Supplemental Table E2; EX1002 ¶201. For these reasons and those

explained with regard to claim 1, *Bégin* discloses all of the elements of claim 5 arranged as in the claim. EX1002 ¶¶191-203. *Bégin* anticipates claims 3 and 5.

3. Claim 17

The elements of claims 17 are set forth above in Section VI.A.3. For the same reasons as set forth above with respect to claim 5, *Bégin* discloses at least one alternative in claim 17, arranged as in the claim, anticipating claim 17. EX1009, Supplemental Table E2; EX1002 ¶¶191-206.

4. Claim 18

The elements of claims 18 are set forth above in Section VI.A.4. *Bégin* discloses that "[d]oses were determined based on weight and total IgE levels." EX1009, Supplemental Table E2. Accordingly, the subjects' weight would have been determined prior to administration of at least the first dose of omalizumab, and *Bégin* meets the added limitation of claim 18. EX1002 ¶207. For this reason and those explained with regard to claim 17, *Bégin* anticipates claim 18. EX1002 ¶¶191-207.

5. Claims 20-21

Claims 20 and 21 depend from claim 17 and further require that the subject is from 1 year to 5 years of age (claim 20), and has an allergy to peanut and to one or more of milk, egg, and cashew (claim 21). *Bégin* discloses that participants were eligible for inclusion if they were "older than or equal to 4 years old" and that the subjects ranged from 4.5-15.4 years of age. Accordingly, *Bégin* meets the

added limitation of claim 20. EX, 1009, 2, Supplemental Table E3; EX1002 ¶208. *Bégin* also discloses that 17 of 25 subjects received OIT treatments with peanut and at least one or more of milk, egg, and cashew, meaning that 15 of the subjects were allergic to peanut and at least one or more of milk, egg, and cashew. *Id.*; EX1002 ¶209. Accordingly, *Bégin* meets the added limitations of claim 21. EX1002 ¶209. For these reasons and those explained with regard to claim 17, *Bégin* anticipates claims 20 and 21. EX1002 ¶¶191-209.

6. Claims 22-23

The elements of claims 22-23 are set forth in Section VI.A.5, above. *Bégin* discloses the following: "The secondary endpoints (i.e. tolerability) were i) the time to reach and maintain doses of 300 mg, 1000 mg and 4000 mg per food allergen protein as well as ii) a 10 fold increase from the baseline reactivity threshold to each of the food allergen proteins." EX1009, 2. *Bégin* further states that "this phase 1 study of rush mOIT provides initial preliminary evidence of increased dose tolerability." *Id.*, 6. Accordingly, *Bégin* meets the added limitations of claim 22. EX1002 ¶¶210-211. Moreover, based on these results, the reduction in allergic reaction would be observed after an accidental exposure, and *Bégin* also meets the added limitations of claim 23. *Id.*

D. Ground 4: Claims 1, 3, 5, 17-18, and 20-24 are Obvious Over *Bégin* (EX1009)

Ground 3 is incorporated by reference. Section VI.C. To the extent *Bégin* fails to anticipate claims 1, 3, 5, 17-18, and 20-24 by failing to explicitly exemplify treating a patient weighing 15 kg, it renders those claims obvious. EX1002 ¶212. The *Bégin* dosing table (Table E2) includes omalizumab dosing amounts/frequencies for patients weighing 15-20 kg, which includes 15 kg patients, and patients with baseline IgE of 30-100, 101-200, and 701-800, all of which are completely within the claimed ranges. EX, 1009, Supplemental Table E2. Based on Table E2, a POSA would have been motivated to treat 15 kg subjects with the following dosing regimen based on their screening/pre-treatment total serum IgE, with a reasonable expectation of success because *Bégin* disclosed that omalizumab increases tolerance to peanut and other food allergens. Accordingly, the following claims reciting the indicated screening IgE, amount, and frequency would have been obvious:

Screening IgE (IU/mL)	Amount (mg)	Frequency	Claims Rendered Obvious
30-100	75	Every 4 weeks	1, 3, 5, 17-18, 20-24
101-300	150	Every 4 weeks	1
701-800	225	Every 2 weeks	1

EX1009, Supplemental Table E2; EX1002 ¶¶213-215; *see Guardant*, 2026 U.S. App. LEXIS 1651, at *11-12.

For the above reasons, including those in Sections I.C.2.d. and VI.C., *Bégin* would have rendered claims 1, 3, 5, 17-18, and 20-24 obvious to a POSA. EX1002 ¶¶212-216.

E. Ground 5: Claims 1-29 are Obvious Over The Combined Teachings of *OUtMATCH-V26* (EX1005), *Arasi* (EX1006), and *PI2021* (EX1007)

1. Summary of Obviousness Arguments

The claims of *US959* all include genera of dosing regimens based on ranges of patient weight and pre-treatment/baseline IgE. If the prior art renders a species of such a genus obvious, it also renders the genus obvious. *See*, *e.g.*, *Aventis Pharma Deutschland GmbH v. Lupin, Ltd.*, 499 F.3d 1293, 1300-3 (Fed. Cir. 2007).

Many of the claims include alternative dosing regimens. Rendering such claims obvious only requires showing that one of the alternatives is obvious. As explained in the Rafi Declaration, each of the alternatives is obvious. The analysis below, however, focuses on one alternative for each such claim.

OUtMATCH-V26 teaches every element of independent claims 1, 12, 17, and 25, except the claimed dosing regimens based on patient weight and pre-treatment/baseline total serum IgE. EX1002 ¶¶124-130; 245-246; Section VI.E.2. (claim 1). For example, *OUtMATCH-V26* teaches:

- Administering omalizumab to treat human subjects having a food allergy (EX1005, 5);
- Subcutaneous administration (*id.*, 6);
- Administering every two or four weeks (*id.*);
- 75 and 150 mg unit doses (*id.*);
- treating subjects 1-55 years of age (*id.*, 5), which includes the claimed subjects weighing ≥10 kg to ≤15 kg;
- dosing based on weight and pretreatment total serum IgE levels per a dosing table (*id.*, 6); and
- determining total serum IgE prior to administering a first dose of omalizumab (*id.*).

EX1002 ¶245. While *OUtMATCH-V26* does not explicitly teach the claimed dosing regimen, it does teach dosing based on weight and pretreatment IgE levels pursuant to a dosing table provided only to investigators. EX1005, 6; EX1002 ¶246. As explained in Section VI.E.2., *Arasi* and *PI2021* teach the missing element, and a POSA would have been motivated to combine the teachings of *OUtMATCH-V26* with the teachings of *Arasi*, and *PI2021* to practice the claimed subject matter with a reasonable expectation of success of obtaining the claimed subject matter. *E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1006 (Fed. Cir. 2018) ("where the general conditions of a claim are disclosed in

the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation") (quoting *In re Aller*, 220 F.2d 454, 456 (C.C.P.A. 1955)).

2. Claims 1, 12, 17, and 25

a. [Claim 1]: "A method of treating a human subject having an allergy to a food allergen, the method comprising: administering to the subject by subcutaneous injection a pharmaceutical composition comprising a dose of omalizumab"

[Claims 12, 17]: "A method of treating a human subject having an allergy to a food allergen, the method comprising: administering to the subject by subcutaneous injection … a pharmaceutical composition comprising a dose of omalizumab"

[Claim 25]: "A method of treating a human subject having an allergy to a food allergen, the method comprising: administering to the subject … by subcutaneous injection … a pharmaceutical composition comprising a dose of omalizumab"

OUtMATCH-V26 taught subcutaneous injection of omalizumab to treat human subjects with food allergies. EX1005, 5, 6 (participants "are allergic to peanut and at least two other foods"), 6 (participants will "receive omalizumab by subcutaneous injection"); EX1002 ¶248. Moreover, subcutaneous injection was the known route of administration of omalizumab. *See* EX1007, 1 ("For subcutaneous (SC) administration only"); EX1002 ¶248 (omalizumab was administered as a subcutaneous injection in, *e.g.*, EX1005, 6; EX1008, 881e.1;

EX1027, 2); Section I.C.1.c. Finally, *PI2021* teaches that omalizumab is provided as part of a pharmaceutical composition when used to treat asthma, and a POSA would have been motivated to use such a composition with a reasonable expectation of success when treating food allergy because it had already been approved as safe and effective for treating an IgE mediated condition. EX1007, 21; EX1002 ¶¶249-250; Section I.C.1.c. Accordingly, it would have been obvious to administer omalizumab subcutaneously to treat food allergy. EX1002 ¶¶247-251.

b. Dosing Regimens Based on Subject Weight and Baseline IgE

Each of independent claims 1, 12, 17, and 25 include dosing regimen limitations presented as alternatives, and thus the prior art need render only one of the alternatives obvious. Accordingly, one alternative from each of those claims is addressed below, but as explained in the Rafi Declaration, each of the alternatives is obvious.

(1) [Claim 1]: "wherein the pharmaceutical composition is administered once about every two weeks and the dose of omalizumab is from 150 mg to 225 mg … and wherein body weight of the subject is equal to or greater than 10 kg and less than or equal to 15 kg, and total serum IgE level of the subject is equal to or greater than 30 IU/ml and less than or equal to 1850 IU/ml"

One of the alternative dosing regimens in independent claim 1 is to treat subjects weighing 10-15 kg with total serum IgE of 30-1850 IU/mL by administering 150 mg to 225 mg of omalizumab once every two weeks. A representative subject with weight and IgE in the midpoint of the claimed ranges, can be determined by averaging the claimed weight and IgE ranges. Such a subject would weigh 12.5 kg (= (10+15)/2) with a serum IgE of 940 IU/mL (= (30+1850)/2). EX1002 ¶¶259-260, 265.

OUtMATCH-V26 studied patients 1-55 years of age in ten U.S. locations. EX1005, 5, 33-35. A POSA would have known that the average weight of 1-5 year-old boys and girls is about 10-18 kg. EX1013-1016; EX1002 ¶254. A POSA therefore would have understood that *OUtMATCH-V26* taught the treatment of, *inter alia*, 10-15 kg subjects. EX1002 ¶254.

The pediatric asthma dosing tables in *PI2021* teach dosing regimens for subjects with total baseline IgE of 30-1300 IU/mL. EX1007, 5 (Table 2). In addition, a POSA would have known that omalizumab had been administered in subjects with a total baseline IgE up to 2,000 IU/mL without any specific safety concern. EX1006, 290. A POSA therefore would have understood that omalizumab could be used safely in subjects having an IgE of 30-1850 IU/mL. EX1002 ¶¶79, 255.

Arasi taught that the majority of studies on omalizumab for treating food allergies determined the dosage and frequency (every 2 or 4 weeks) based on subject weight and total serum IgE, according to the asthma and nasal polyps indication in the XOLAIR labeling. EX1006, 289-290; EX1002 ¶137. *PI2021* taught that in asthma clinical trials, "[p]atients were treated according to a dosing table to administer at least 0.016 mg/kg/IU (IgE/mL) of XOLAIR … over each 4-week period." EX1007, 24; EX1002 ¶142. *See also* Section I.C.2.b., I.C.2.e..

Following *OUtMATCH-V26*, a POSA therefore would have been motivated to calculate the four week dosage by applying the prior art formula:

4-week dose = at least 0.016 mg x weight (kg) x total serum IgE (IU/mL)

EX1002 ¶¶76, 224, 232-244. For the representative subject, i.e., 12.5 kg/940 IgE, the four-week dose would be at least 188 mg (0.016 x 12.5 x 940). As noted above and pursuant to the then-approved labeling for omalizumab, omalizumab could also be dosed every two weeks (Section I.C.2.e.), and a POSA would have calculated the two week dosage to be at least 94 mg (188/2). Because *OutMATCH-V26* and *PI2021* teach that omalizumab is supplied in only 75 and 150 mg pre-filled syringes, and the *PI2021* dosing table instructs administration in increments of 75 mg, a POSA would have been motivated to give those doses in 75 mg increments. Thus, the four week dose of ***at least*** 188 mg would be given as 225 mg (the

next highest 75 mg increment), and the two week dose of ***at least*** 94 mg would be given as 150 mg (the next highest 75 mg increment). Since a POSA only has to choose between two predictable solutions, it would have been obvious to a POSA to administer 150 mg of omalizumab every two weeks to a subject weighing 10-15 kg having a total serum IgE of 30-1850 IU/mL. EX1002 ¶¶232-244, 259-263. *See In re Kubin*, 561 F.3d 1351, 1361 (Fed. Cir. 2009) ("KSR posits a situation with a finite, and in the context of the art, small or easily traversed, number of options that would convince an ordinarily skilled artisan of obviousness") (quoting *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008)).

(2) **[Claim 12, 17]: "administering to the subject by subcutaneous injection once about every two weeks a pharmaceutical composition comprising a dose of omalizumab of: 150 mg when body weight of the subject is equal to or greater than 10 kg and less than or equal to 12 kg, and total serum IgE level of the subject is greater than 600 IU/ml and less than or equal to 1500 IU/ml"**

[Claim 25] "administering to the subject having a body weight equal to or greater than 10 kg and less than or equal to 12 kg by subcutaneous injection a pharmaceutical composition comprising a dose of omalizumab of: … 150 mg once about every two weeks if total serum IgE level of the subject is greater than 600 IU/ml and less than or equal to 1500 IU/ml;

One of the alternative dosing regimens in independent claims 12, 17, and 25, is to treat subjects weighing 10-12 kg with total serum IgE of greater than 600 to less than or equal to 1500 IU/mL by administering 150 mg of omalizumab once every two weeks. A representative subject within those claimed ranges would weigh 11 kg with a serum IgE of 1050 IU/mL. EX1002 ¶¶329, 344, 359.

As explained above, *OUtMATCH-V26* would have included studying 1-5 year-old boys and girls with average weights of about 10-18 kg. EX1005, 5; EX1013-1016; EX1002 ¶254. A POSA therefore would have understood that *OUtMATCH-V26* taught the treatment of 11 kg subjects. EX1002 ¶254. As explained in Section VI.E.2.b.(1) for claim 1, based on the teachings of *PI2021* and *Arasi*, a POSA would have understood that omalizumab could be used safely in subjects having an IgE of 30-1850, which includes the claimed greater than 600 to 1500 IU/mL. EX1007, 5 (Table 2); EX1006, 290; EX1002 ¶255.

For the same reasons as set forth above with respect to claim 1, a POSA would have determined the following four and two week doses for a representative subject (i.e., 11 kg/1050 IgE) by using the algorithm taught in *PI2021*:

- 4-week dose: at least 184.8 mg (0.016 x 11 x 1050), given as 225 mg (next highest 75 mg increment); and
- 2-week dose: at least 92.4 mg (184.8/2), given as 150 mg (next highest 75 mg increment).

EX1002 ¶¶232-244, 329, 344, 359.

Accordingly, it would have been obvious to a POSA to administer 150 mg of omalizumab, every two weeks, to a subject weighing 10-12 kg having a total serum IgE of greater than 600 to 1500 IU/mL. *Id.* ¶¶334, 345, 360. *Kubin*, 561 F.3d at 1361.

(3) [Claims 12, 17, and 25]: "wherein the total serum IgE level of the subject is determined prior to administration of a first dose of omalizumab."

OUtMATCH-V26 states that the omalizumab "dose administered and the dosing interval are determined by serum total IgE level and body weight (measured before the start of treatment) per the study drug dosing table." EX1005, 6. Likewise, *PI2021* taught, when treating asthma with omalizumab, to "[d]etermine dose (mg) and dosing frequency by serum total IgE level (IU/mL) ***measured before the start of treatment***, and body weight (kg)" (EX1007, 1, 3, 4 (emphasis added)), and taught that due to the formation of omalizumab-IgE complexes that are eliminated from the body more slowly than free IgE, serum total IgE levels (bound and unbound) increase after the first dose (*id.*, 22). Accordingly, a POSA would have been motivated to determine serum total IgE levels before starting

treatment in order to determine the appropriate dose and dosing frequency. EX1002 ¶¶335, 350, 361.

c. A POSA Would Have Been Motivated to Practice the Subject Matter of Claims 1, 12, 17, and 25 with a Reasonable Expectation of Success

A POSA would have been motivated to combine the teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* for the following reasons. As noted in Section VI.E.1., above, *OUtMATCH-V26* taught all the elements of independent claim 1, 12, 17, and 25, except the specifically claimed dosage regimen. *Arasi* summarized the state of research on using omalizumab to treat food allergies, including discussion of the ongoing OUtMATCH study. *Arasi* also stated that the majority of studies of omalizumab report using a dose/frequency based on subject weight and total serum IgE, "according to asthma and nasal polyps indication." The label, *PI2021* provided Genentech's omalizumab dosing and administration regimens for asthma and nasal polyps at the time of invention. A POSA would have reasonably expected the combined teachings to work in view of the long history of safe and effective use of omalizumab, its breakthrough therapy designation, and the fact that as of the publication of *OutMATCH-V26*, the OUtMATCH clinical study had been ongoing for almost three years (July 2019 – May 2022). *See*, *e.g.*, EX1017 (IND down to two years of age based on over a decade of omalizumab safety data); EX1008, EX1009, EX1039 (demonstrating

safety and efficacy of omalizumab in combination with OIT); EX1006 (omalizumab monotherapy effective to treat food allergy in asthma patients); Section I.C.1.c.; EX1002 ¶¶219-231, 250, 267-271, 315, 324-362.

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For the above reasons, the combined teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* would have rendered claims 1, 12, 17, and 25 obvious to a POSA. EX1002 ¶¶245-272; 324-362.

3. Claim 2

Claim 2 depends from claim 1 and recites additional alternative dosing regimens, one of which is the same as the alternative dosing regimen addressed in the analysis of claims 12, 17, and 25 in Section VI.E.2.b.(2)., i.e.: administering 150 mg of omalizumab every two weeks to a subject weighing 10-12 kg with total serum IgE of greater than 600 to 1500 IU/ml determined prior to a first dose of omalizumab. For the same reasons as set forth above with respect to claims 12, 17, and 25, the combined teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* would have rendered claim 2 obvious to a POSA. EX1002 ¶¶273-285.

4. Claims 3 and 11

Claim 3 depends from claim 1 and recites the following dosing regimen: administering 75 mg of omalizumab every four weeks to a subject weighing 10-15 kg with total serum IgE of 30-300 IU/ml determined prior to a first dose of

omalizumab. Claim 11 depends from claim 1 a recites the same dosing regimen as one of its alternatives. For the same reasons as in Section VI.E.2. with respect to claim 1, a POSA would have determined the following doses for a representative subject, i.e., 12.5 kg/165 IgE, by using the algorithm taught in *PI2021*:

- 4 week dose: at least 33 mg (0.016 x 12.5 x 165), given as 75 mg (smallest dose); and
- 2 week dose: at least 16.5 mg (33/2), given as 75 mg (smallest dose).

EX1002 ¶¶287, 318.

Accordingly, it would have been obvious to a POSA to administer 75 mg of omalizumab, every four weeks, to a subject weighing 10-15 kg having a total serum IgE of 30-300 IU/mL, and the combined teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* would have rendered claims 3 and 11 obvious to a POSA. *Id.*, ¶¶286-290, 316-323. *Kubin*, 561 F.3d at 1361.

5. Claim 4

Claim 4 depends from claim 1 and recites the following dosing regimen: administering 150 mg of omalizumab every four weeks to a subject weighing 10-15 kg with total serum IgE of greater than 300 and less than or equal to 600 IU/ml determined prior to a first dose of omalizumab. For the same reasons as in Section VI.E.2. with respect to claim 1, a POSA would have determined the following

doses for a representative subject, i.e., 12.5 kg/450 IgE, by using the algorithm taught in *PI2021*:

- 4 week dose: at least 90 mg (0.016 x 12.5 x 450), given as 150 mg (next highest 75 mg increment); and
- 2 week dose: at least 45 mg (90/2), given as 75 mg (smallest dose).

EX1002 ¶292.

Accordingly, it would have been obvious to a POSA to administer 150 mg of omalizumab, every four weeks, to a subject weighing 10-15 kg having a total serum IgE of greater than 300 to 600 IU/mL, and the combined teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* would have rendered claim 4 obvious to a POSA. *Id.*, ¶¶291-295. *Kubin*, 561 F.3d at 1361.

6. Claim 5

Claim 5 depends from claim 1 and recites four additional dosing regimen alternatives, including the following: administering 75 mg of omalizumab every four weeks to a subject weighing greater than 12 to less than or equal to 15 kg with total serum IgE of 30-300 IU/ml determined prior to a first dose of omalizumab. For the same reasons as in Section VI.E.2. with respect to claim 1, a POSA would have determined the following doses for a representative subject, i.e., 13.5 kg/165 IgE, by using the algorithm taught in *PI2021*:

- 4 week dose: at least 35.6 mg (0.016 x 13.5 x 165), given as 75 mg (smallest dose); and
- 2 week dose: at least 17.8 mg (35.6/2), given as 75 mg (smallest dose).

EX1002 ¶298.

Accordingly, it would have been obvious to a POSA to administer 75 mg of omalizumab, every four weeks, to a subject weighing greater than 12 kg to 15 kg having a total serum IgE of 30-300 IU/mL, and the combined teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* would have rendered claim 5 obvious to a POSA. *Id.*, ¶¶296-307. *Kubin*, 561 F.3d at 1361.

7. Claim 10

Claim 10 depends from claim 1 and recites two additional dosing regimen alternatives, including the following: administering 150 mg of omalizumab every two weeks to a subject weighing greater 10-12 kg with total serum IgE of treater than 1200 to less than or equal to 1500 IU/ml determined prior to a first dose of omalizumab. For the same reasons as in Section VI.E.2. with respect to claim 1, a POSA would have determined the following doses for a representative subject, i.e., 11 kg/1350 IgE, by using the algorithm taught in *PI2021*:

- 4 week dose: at least 237.6 mg (0.016 x 11 x 1350), given as 300 mg (next highest 75 mg increment); and
- 2 week dose: at least 118.8 mg (237.6/2), given as 150 mg (next highest 75 mg increment).

EX1002 ¶312.

Accordingly, it would have been obvious to a POSA to administer 150 mg of omalizumab, every four weeks, to a subject weighing 10-12 kg having a total serum IgE of greater than 1200 to 1500 IU/mL, and the combined teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* would have rendered claim 10 obvious to a POSA. *Id.*, ¶¶308-315. *Kubin*, 561 F.3d at 1361.

8. Claims 6, 13, 18, and 26

Claims 6, 13, 18, and 26 depend from claims 2, 12, 17, and 25, respectively, and further require that the body weight of the subject is determined prior to administration of a first dose of omalizumab. Because determining a minimum dosage amount requires knowing a subject's body weight, a POSA would have had reason to determine a subject's body weight prior to administration of such first dose in order to determine the appropriate dose and dosing schedule. For these reasons and the reasons in Sections VI.E.2. and VI.E.3. regarding claims 2, 12, 17, and 25, the combined teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* would have rendered obvious claims 6, 13, 18, and 26. EX1002 ¶¶363-366.

9. Claims 7, 16, 19, and 29

Claims 7, 16, 19, and 29 depend from claims 2, 12, 17, and 25, respectively, and further require that the subject is not receiving concurrent OIT. *Arasi* is titled "Omalizumab as monotherapy for food allergy" and discloses several studies that "support[] the use of Omalizumab as monotherapy in food allergy." EX1006, 288; EX1002 ¶¶131, 138, 368. The monotherapy studies discussed in *Arasi* include *Fiocchi 2019*, a 2019 retrospective observational study of 15 pediatric patients. EX1006, 288. Regarding *Fiocchi 2019*, *Arasi* states that "[a]fter 4 months of Omalizumab treatment, all patients experienced an increase in their eliciting threshold to each food tested," that 11 patients "asymptomatically consumed the full challenge amount," and that the results "represent[ed] a statistically significant improvement for egg, milk, baked milk, and wheat." EX1006, 288; EX1002 ¶368. In addition, *OUtMATCH-V26* included an omalizumab monotherapy arm. EX1005, 6; EX1002 ¶369. As explained in *Arasi*, "in its phase 1 the [OUtMATCH] design is a simple Omalizumab/placebo comparison." EX1006, 289. Based on *Arasi* and *OUtMATCH-V26*, a POSA would have been motivated to use omalizumab as a monotherapy to treat food allergy with a reasonable expectation of success. EX1002 ¶370. For these reasons and the reasons in Sections VI.E.2. and VI.E.3. regarding claims 2, 12, 17, and 25, the combined

teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* would have rendered obvious claims 7, 16, 19, and 29. Section I.C.1.c.; EX1002 ¶¶367-371.

10. Claims 8, 15, 22, 23, and 28

Claim 22 depends from claim 17 and further requires that the treating comprises reducing an allergic reaction following exposure of the subject to the food allergen. A POSA would have understood that such exposure would include accidental exposure. EX1002 ¶372. Claims 8, 15, 23, and 28 depend from claims 2, 12, 22, and 25, respectively, and further require that the treating comprises reducing an allergic reaction following accidental exposure of the subject to the food allergen. Based on *OUtMATCH-V26* and the studies described in *Arasi*, which report that patients in omalizumab monotherapy studies experienced large, statistically significant increases in tolerated doses of food allergens compared to baseline, a POSA would have reasonably expected that treatment with omalizumab in accordance with the claimed amounts and frequencies would reduce an allergic reaction following accidental exposure of a subject to a food allergen. EX1006, 288; EX1002 ¶373. For these reasons and the reasons in Sections VI.E.2. and VI.E.3. regarding claims 2, 12, 17, and 25, the combined teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* would have rendered obvious claims 15, 22, 23, and 28. EX1002 ¶¶372-374.

11. Claims 9, 14, 24, and 27

Claims 9, 14, 24, and 27 depend from claims 2, 12, 22, and 25, respectively, and further require that the treating comprises reducing a moderate-to-severe allergic reaction following exposure of the subject to the food allergen. *Arasi* states that "FDA granted Breakthrough Therapy Designation for Omalizumab for the prevention of severe allergic reactions following accidental exposure to one or more foods in people with allergies." EX1006, 290. Based on *OUtMATCH-V26* and *Arasi*, a POSA would have reasonably expected that treatment with omalizumab in accordance with the claimed amounts/frequencies would reduce a moderate-to-severe allergic reaction following exposure of a subject to a food allergen. EX1002 ¶375. This reasonable expectation would have been bolstered by a POSA's further knowledge that when omalizumab was administered to six children who had "severe asthma and anaphylactic reactions to two or more foods," it was well tolerated in all children, five of six children developed full tolerance to at least one specific food, and the sixth child showed an increase of over 80% in tolerance to milk and egg. EX1010, 15 (A42); EX1002 ¶114. For these reasons and the reasons in Sections VI.E.2. and VI.E.3. regarding claims 2, 12, 22, and 25, the combined teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* would have rendered obvious claims 9, 14, 24, and 27. EX1002 ¶¶375-377.

12. Claim 20

Claim 20 depends from claim 17 and further requires that the subject is from one year to five years of age. As explained above, a POSA would have been motivated to use omalizumab to treat subjects one to five years of age because OUtMATCH was designed to include subjects as young as 1 year of age. EX1005, 5; EX1002 ¶380. In addition, food allergy was known to impact 1-10% of infants and pre-school aged children and to be the main etiology of anaphylaxis in children. EX1002 ¶379. Accordingly, *OUtMATCH-V26* in view of *Arasi* would have motivated a POSA to use omalizumab to treat infants and pre-school aged children, which would include subjects from one to five years of age, with a reasonable expectation of success. *See* EX1005, 5; EX1002 ¶381. Indeed, as a POSA would have been aware, omalizumab had been used safely in infants and pre-school aged students. *See*, *e.g.*, EX1017, 3, 6 (2-3 years old); EX1040, 1 (3-13 years old); EX1022, 1 (4-15 years old). For these reasons and the reasons in Section VI.E.2. regarding claim 17, the combined teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* would have rendered obvious claim 20. EX1002 ¶¶378-382.

13. Claim 21

Claim 21 depends from claim 17 and further requires that the subject has an allergy to peanut and to one or more of milk, egg, and cashew. *OUtMATCH-V26* states that it is a study of subjects "allergic to peanut and at least two other foods

(including milk, egg, wheat, cashew, hazelnut, or walnut)." EX1005, 5, 31. *Arasi* describes omalizumab monotherapy studies in subjects having peanut allergies (*Sampson*) and in subjects having, *inter alia*, milk and egg allergies (*Fiocchi 2019*), and describes those studies as observing reduced allergic responses in the subjects after receiving omalizumab. EX1006, 288. For these reasons and the reasons set forth in Section VI.E.2. regarding claim 17, the combined teachings of *OUtMATCH-V26*, *Arasi*, and *PI2021* would have rendered obvious claim 20. EX1002 ¶¶383-385.

F. Objective Indicia of Non-Obviousness

Petitioner is not aware of any relevant objective indicia of non-obviousness that have a nexus to, or are commensurate in scope with, any of the challenged claims. EX1002 ¶386. Petitioner reserves the right to respond to any allegations that objective indicia support the validity of the challenged claims.

G. Discretion Under §325(d) and §314

Consistent with the guidance provided by "FAQs for Interim Processes for PTAB Workload Management," Petitioner does not present affirmative arguments as to discretionary denial. Should Patent Owner elect to file a Discretionary Denial Brief, Petitioner will present arguments in its Opposition to that brief,

VII. CONCLUSION

For the reasons set forth above, claims 1-29 of *US959* are unpatentable. Petitioner requests that an *inter partes* review of these claims be instituted and that the claims be cancelled.

Respectfully submitted,

Dated: May 26, 2026

/ Lora M. Green /
Lora M. Green, Lead Counsel
Reg. No. 43,541

VIII. APPENDIX – LIST OF EXHIBITS CITED

Exhibit No.	Description
1001	U.S. Patent No. 12,030,959 to Owen et al. (July 9, 2024) ("*US959*")
1002	Declaration of Dr. Asif Rafi in Support of Petition for Inter Partes Review of U.S. Patent No. 12,030,959
1003	*Curriculum Vitae* of Dr. Asif Rafi
1004	Excerpts of prosecution history of U.S. Application No. 18/486,053, now U.S. Patent No. 12,030,959
1005	NCT03881696, *Omalizumab as Monotherapy and as Adjunct Therapy to Multi-Allergen OIT in Food Allergic Participants*, U.S. NATIONAL LIBRARY OF MEDICINE, CLINICALTRIALS.GOV (Version 26, May 2, 2022), https://clinicaltrials.gov/study/NCT03881696?tab=history&a=26#version-content-panel ("*OUtMATCH-V26*")
1006	Stefanie Arasi et al., *Omalizumab as monotherapy for food allergy*, 21 CURR. OPIN. ALLERGY CLIN. IMMUNOL. 286-291 (June 2021) ("*Arasi*")
1007	*XOLAIR® Prescribing Information*, FOOD AND DRUG ADMINISTRATION (July 2021), https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/103976s5239lbl.pdf ("*PI2021*")
1008	Andrew J. MacGinnitie et al., *Omalizumab facilitates rapid oral desensitization for peanut allergy*, 139 J. ALLERGY CLIN. IMMUNOL. 873-881.e8 (2016) ("*MacGinnitie*")
1009	Phillipe Bégin et al., *Phase 1 results of safety and tolerability in a rush oral immunotherapy protocol to multiple foods using Omalizumab*, 10:7 ALLERGY ASTHMA & CLIN. IMMUNOL. 1-10s.3 (2014) ("*Bégin*")
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IX. CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. §42.24(d), the undersigned certifies that this Petition complies with the type-volume limitation of 37 C.F.R. §42.24(a). The word count application of the word processing program used to prepare this Petition indicates that the Petition contains 13,782 words, excluding the parts of the brief exempted by 37 C.F.R. §42.24(a).

Respectfully submitted,

Dated: May 26, 2026

/ Lora M. Green /
Lora M. Green, Lead Counsel
Reg. No. 43,541

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. §§42.6(e) and 42.105(a), this is to certify that I caused to be served a true and correct copy of the foregoing Petition for Inter Partes Review (and accompanying Exhibits 1001 through 1033 and Exhibits 1035 through 1053) by USPS Priority Express Delivery, on this 26th day of May, 2026, on the Patent Owner at the correspondence address of the Patent Owner Counsel as follows:

Respectfully submitted,

Dated: May 26, 2026

/ Ashley F. Cheung/
Paralegal for Petitioner's Counsel