IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF TEXAS
FORT WORTH DIVISION

OUTSOURCING FACILITIES ASSOCIATION, ET AL.,

Plaintiffs,

v. **No. 4:24-CV-0953-P**

UNITED STATES FOOD AND DRUG ADMINISTRATION, ET AL.,

Defendants.

***Amicus Curiae* Brief of Ivim Health**
In Support of Plaintiffs' Motion for a Preliminary Injunction

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Ivim Health is a medical institution that employs nearly 100 medical providers, including board certified physicians from the American Board of Obesity Medicine (ABOM) and nurse practitioners trained by our obesity medicine staff, dedicated to the treatment and management of obesity, weight-related conditions, and overall optimization of health and wellness. Ivim Health specializes in the clinical application of innovative approaches to weight-loss therapy, including the use of glucagon-like peptide-1 (GLP-1) medications such as Novo Nordisk's Wegovy® and Ozempic®, Eli Lilly's Zepbound® and Mounjaro®, and safe and effective clinical alternatives such as compounded semaglutide and compounded tirzepatide from FDA-regulated, state-licensed compounding pharmacies.

Ivim Health has no financial interests or relationships with Eli Lilly, any other biopharmaceutical company, the Outsourcing Facility Association (OFA), or North American Custom Laboratories, LLC. Ivim Health does not produce, manufacture, or dispense compounded medications, nor does it own or operate any manufacturing facility or pharmacy. Ivim Health's sole focus is always on the health and well-being of patients, ensuring access to necessary treatments, and maintaining continuity of care for those patients currently relying on these treatments. Ivim Health respectfully submits this brief as medical providers, in unwavering support of continued access for the patients reliant upon tirzepatide therapy whose health and wellness could be severely impacted by an adverse ruling on the Plaintiffs' motion.

Ivim Health's interest is in providing the Court with a perspective from a medical institution whose medical providers are experts in the field of obesity medicine and who work clinically with patients impacted by accessibility barriers to GLP-1 medications, including Eli Lilly's Mounjaro® and Zepbound®. Ivim Health has unique insight into the issues presented in

this litigation as a medical institution that prescribes both branded and compounded medications. The choice of drug therapy is dependent upon a patient's personalized medical needs and accessibility to medications. Our goal is to provide professional and clinical insight into the inequities that result when a shortage of medication occurs, and the critical role that compounded medications have played clinically in the current shortage of branded GLP-1 medications. From our clinical experience, Ivim Health understands how important it is for patients to have continuous access to the most effective weight loss therapies available. Ivim Health's medical providers have experienced first-hand how GLP-1 drug shortages have impacted its patients. Ivim Health's physicians and nurse practitioners have the clinical expertise to understand and explain how, absent injunctive relief, FDA's recent decision (ECF No. 65-1, at 2 ("Decision")) will lead to significant patient harm through the reversal of the positive health benefits provided by GLP-1 medications if patients are forced to discontinue treatment with compound tirzepatide. FDA's decision to declare the shortage of tirzepatide "resolved" is contrary to Ivim Health's experience and raises significant patient health concerns due to the inaccessibility of Eli Lilly's Mounjaro® and Zepbound®.

Ivim Health respectfully submits that, in reviewing the challenge to FDA's action, it is important to recognize the negative, adverse health impact an abrupt discontinuation of GLP-1 therapy will have on patients reliant on tirzepatide. Moreover, in considering the preliminary injunction factors, Ivim Health further submits that the Court should consider the time it takes for patients to adjust to a new treatment regimen where a former regimen has been removed as a treatment option. This loss of access will likely disproportionately affect vulnerable patient populations, especially those of lower socioeconomic status and those in rural regions in which supply issues of tirzepatide may be more prevalent. This amplifies the importance that the Court

hold FDA accountable to take the time to receive the robust inputs necessary from all interested parties prior to making such an important decision. Ivim Health hopes that its unique perspective will assist the Court in determining that FDA's process and decision were not consistent with the law and did not adequately consider the irreparable harm to patients currently on tirzepatide therapy, as well as to the American public at large.

INTRODUCTION

Good health is not a luxury—it is essential to one's quality of living. For Ivim Health, the relationship between our team of medical providers and the over 600,000 Americans who have sought our medical services survives on this belief. A true patient-provider relationship extends beyond an encounter and a prescription; it is a partnership devoted to optimizing health and well-being. Together, the provider and patient work to craft an individualized treatment plan that fits the patient's medical needs. Any disruption in the ability to provide necessary treatment jeopardizes this relationship, undermines the medical provider's approach to treatment, and impacts the success of both the medical partnership and patient health outcomes.

As medical providers devoted to helping patients achieve a better quality of life as they manage conditions like diabetes, obesity, and other weight-related conditions, we at Ivim Health have seen firsthand the promise of innovative GLP-1 medications like tirzepatide. Unfortunately, we have also seen the negative health outcomes of ongoing barriers to patient access. Patients who would undoubtably benefit clinically from uninterrupted GLP-1 treatment continue to struggle to find pharmacies with reliable supply of Mounjaro® and Zepbound®, despite assertions by Eli Lilly that it can now adequately supply the market.

During a period of undisputed shortage for branded tirzepatide, compounded versions of tirzepatide have substantially helped to fill the gap for many patients, providing them access to life-changing treatment programs that would otherwise be out of reach. This is precisely as it should be, as compounded medicines play a critical role in our healthcare system in facilitating patient access, especially in the event of a drug shortage. Under Sections 503A and 503B of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 301 *et seq.* Congress regulates pharmacy compounding while exempting compounded drugs from premarketing review. And by

providing that compounding is appropriate for drugs designated to be in shortage, Congress recognized that compounded drugs help to "bring certainty to the drug supply chain and ensure that patients will continue to receive the medicine that they need without interruption." 159 CONG. REC. H5946-02 (Sept. 28, 2013) (statement of Rep. Upton).

With this context in mind, determinations by FDA that a shortage has resolved require careful attention and scrutiny. This decision carries the potential to inadvertently restrict patient access by removing market availability of compounded medicines as a safety valve. This is not a judgment FDA can afford to get wrong as it will have a direct and negative impact on patient health outcomes. If a shortage is declared resolved, despite significant ongoing issues with reliable supply, patients who have been successfully using compounded medicines will suddenly lose access, depriving them of continuity of care and risking reversal of their health gains. Given these high stakes, it is important for FDA to err on the side of caution, provide for a review process that meaningfully considers information from a full spectrum of relevant stakeholders (beyond just the branded manufacturer), and provide an adequate timeline for medical providers and their patients to plan a transition of therapy to available options.

In our professional and clinical opinion, the previous FDA Administration fell short of those objectives, as it elected to remove tirzepatide from shortage designation without full input from community stakeholders like Ivim Health and its patients. Restricting access in the face of ongoing shortages poses a threat to patient safety inconsistent with Congress's protective aims. An open notice and comment process would have involved members of the public, such as patients who are directly impacted by the lack of access to branded tirzepatide, doctors who seek to aid them, pharmacies who seek to fulfill their medication, and telehealth providers like Ivim Health who are experts in this space and provide medical care to this patient population at scale. The

specific choices and assumptions FDA made about the shortage could have been addressed and engaged more fully, and FDA should have demanded compelling evidence before the agency removed Mounjaro® and Zepbound® from the drug shortage list.

Continued and reliable access to tirzepatide medicines is essential for patients and well within the public interest for courts to protect. Even a temporary loss of access or restriction of medical providers to optimally personalize dosing and titration due to supply constraints would have significant negative health outcomes for patients, given the importance of continuity of treatment. In addition, even a short duration of loss of access may require providers to reset the patient's medication titration. Patients who miss two or more doses are at significantly higher risk of having adverse side effects upon re-initiation of therapy. Even short durations of supply chain issues can therefore have significant therapeutic impact.

Finally, if access to safe, regulated, compounded medicines is prematurely blocked and Eli Lilly's products are not made broadly available to patients, there is a significant risk that patients will turn to unregulated and harmful alternatives, including counterfeit products and research-grade products. Removing compounding as a safe, regulated, and accessible source for patients to obtain tirzepatide will further the negative health consequences that result from the use of unregulated and dangerous products.

As a healthcare institution invested in the outcomes of its patients, Ivim Health seeks to avoid adverse, long-term health consequences that would be caused by an abrupt loss of patient access from FDA's procedurally and substantively deficient decision. Action should be taken to prevent potential irreparable harm, and we ask the Court to ensure adequate protection of the health of the American people by granting the Plaintiffs' motion for a preliminary injunction.

ARGUMENT

I. Compounded medicines provide a critical safety valve in the health care system to facilitate patient access to safe and effective treatments.

A. An FDA "shortage" decision must account for the critical role compounded medicines may serve in protecting patient access.

Pharmacy compounding of medications is "as old as time." Ross C. Reggio, *FDA Overreach: Is Your Pet's Health A "Major Question" to You?*, 81 WASH. & LEE L. REV. 907 (2024). For millennia, pharmacists have used compounding practices to produce individualized medications that meet patients' specific needs. *See Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 361 (2002) (describing compounding as "a traditional component of the practice of pharmacy"). Most pharmacy schools teach compounding as part of their standard curriculum, and some states even require all licensed pharmacies to offer compounding services. *Id.* Compounded medications are important to facilitate patient access: among other things, compounding allows a pharmacist to switch an ingredient in a mass-produced product to account for an allergic reaction, change a product's dosage form (*e.g.*, to avoid difficulties with swallowing), or alter a product's formulation to prevent a patient from receiving too much or too little of a drug.

Reflecting this history, Congress has long recognized the importance of compounded medicines to fill the gaps in patient access and ensure individuals receive the medication they require. Section 503A of the FDCA regulates pharmacy compounding and exempts compounded drugs from needing approval by FDA and other state agencies before the medications can be sold. *See* 21 U.S.C. § 353a; *Allergan USA Inc. v. Imprimis Pharms., Inc.*, No. 17-cv-1551, 2017 WL 10526121, at *2 (C.D. Cal. Nov. 14, 2017). And for nearly 50 years after the enactment of the FDCA and Section 503A, FDA "generally left regulation of compounding to the States." *Thompson*, 535 U.S. at 362. However, as compounding medication production became more sophisticated, with increases in scale that could reach more patients, Congress and FDA became

more involved in regulating compounding medications, continuing to ensure their safety and accessibility for patients.

In 2013, Congress enacted the Drug Quality and Security Act, which amended 503A and added Section 503B to the FDCA. *See* 21 U.S.C. § 353b. Section 503B created a "new category of drug maker called an 'outsourcing facility,'" which are facilities "permitted to sell bulk compounded drug products to health care practitioners and hospitals as 'office stock,' for providers to have available and to use on an as-needed basis" per their discretion. *Athenex Inc. v. Azar*, 397 F. Supp. 3d 56, 59 (D.D.C. 2019). In passing the law, Congress sought to "bring certainty to the drug supply chain and ensure that patients will continue to receive the medicine that they need without interruption." 159 CONG. REC. H5946-02 (Sept. 28, 2013) (statement of Rep. Upton). Additionally, Congress aimed for 503B "to protect American families against counterfeit drugs . . . eliminate[] and prevent[] increases in drug prices [and] avoid[] additional drug shortages." *Id.*

Consistent with these legislative objectives, Section 503B authorizes compounding using bulk drug substances that "appear[] on the drug shortage list in effect under section 356e" of the FDCA. 21 U.S.C. §§ 353b(a)(2)(A)(ii), (a)(5), (d)(2)(A); *see* 21 U.S.C. § 356e (describing the Secretary's obligation to "maintain an up-to-date list of drugs that are determined by the Secretary to be in shortage in the United States"). Section 503A similarly provides that only when the relevant drug product is "commercially available" do limits apply on the scale of pharmacy compounding of drug products that "are essentially copies" of approved drugs. 21 U.S.C. § 353a(b)(1)(D). These provisions reinforce Congress's central concern in ensuring that patients are always able "to receive the medicine that they need without interruption." 159 CONG. REC. H5946-02 (Sept. 28, 2013) (statement of Rep. Upton).

FDA's determination that a shortage has abated must account for Congress's objectives regarding patient access, in recognition of the fact that prematurely declaring a shortage over will limit the availability of compounding medicines as a safety valve to increase supply. The relevant question for FDA is not merely whether the manufacturer of a branded drug product has taken some steps to increase production or pledged to meet future demand as the single source for a critical medicine. In the face of evidence regarding ongoing problems for lack of access, FDA should not rely on a brand manufacturer's pledges regarding future capacity and projection that problems will eventually abate. Restricting access in the face of ongoing disruptions for patients poses a threat to patient safety that is inconsistent with Congress's objective to maintain a stable drug supply chain. A drug shortage does not truly abate until there is objective evidence of reliable, ongoing supply and distribution that ensures patients "receive the medicine that they need without interruption." 159 CONG. REC. H5946-02 (Sept. 28, 2013) (statement of Rep. Upton).

B. Compounded medicines have served as a critical safety valve for patient access to tirzepatide, which FDA's shortage decision threatens to jeopardize.

For the last several years, compounding has served a critical role in providing patients with access to tirzepatide—a breakthrough therapy for the treatment and management of obesity. At Ivim Health, tirzepatide is seen as the gold standard for medical weight loss based on safety and efficacy data presented in clinical trials evaluating tirzepatide for the treatment of obesity or being overweight. Tirzepatide is helping to transform patients' lives, but it has been notoriously difficult for patients and their providers to obtain reliable access to this treatment. Compounding pharmacies have played a critical role in alleviating the shortfall, and Ivim Health is gravely concerned that FDA's decision to remove tirzepatide from its drug shortage list will jeopardize patient access. Based on Ivim Health's experience working with patients and interfacing with pharmacies, Ivim Health is concerned that there have been and remain significant barriers to

access that have not sufficiently abated, notwithstanding FDA's decision removing the product from its shortage list.

Ivim Health's recent experience runs counter to FDA's contention that the tirzepatide shortage has been "resolved." Decision at 2. For example, since October 2024, over 10% of the patients who were prescribed Zepbound® and Mounjaro® from Ivim Health were unable to fill their orders *at all* or at *any* retail or mail-order pharmacy in the country, or even through the Lilly Direct program (which is supposed to allow direct patient purchasing from Eli Lilly). Similarly, during that same period, 15% of all patients prescribed Zepbound® and Mounjaro® by Ivim Health had their prescriptions rejected by at least one retail or mail order pharmacy. Or put another way, since FDA's initial determination decision, a significant percentage of patients prescribed Zepbound® and Mounjaro® by Ivim Health medical providers have continued to have issues with accessing their branded tirzepatide medications.

In addition, due to supply constraints, three major mail order pharmacies continue to have significant issues with access to branded tirzepatide products:

- Optum Home Pharmacy informed Ivim Health as late as November 1, 2024 that it would no longer be accepting new patients on Eli Lilly's Zepbound®. Ivim Health has confirmed that this shortage persists.
- Express Scripts Pharmacy continues not to accept new patients for home delivery of GLP-1 therapies. Ivim Health has confirmed that these shortages persist.
- On May 15, 2024, CVS Caremark Mail Service Pharmacy declared it had run out of inventory of Eli Lilly's Mounjaro® and three other branded GLP-1 medications. Ivim Health has confirmed that these shortages persist.

Faced with these ongoing issues with access to branded tirzepatide products, Ivim Health medical providers have continued to prescribe compounded tirzepatide from reputable

compounding pharmacies to fulfill these patients' unmet needs. FDA's decision threatens to leave such patients without treatment options, substantially disrupting their care.

In its decision, FDA acknowledged there is evidence of patients continuing to encounter challenges in getting prescriptions filled for Mounjaro® and Zepbound®, and that some pharmacies lack "ample stock of these tirzepatide products. . . at certain points in time." Decision at 18. Nonetheless, they concluded that "Lilly's supply is now meeting or exceeding demand nationally." *Id*. Respectfully, minimizing ongoing access challenges as transitory based on optimistic Eli Lilly projections creates significant health risk for patients. Disruptions within the supply chain risk devastating consequences for patients. These consequences will not be avoided with assurances that problems will eventually work themselves out over time.

II. FDA's decision removing tirzepatide from shortage designation without notice and comment deprived the agency of the full range of information needed.

As explained in Plaintiffs' opening brief, FDA made its decision to remove tirzepatide from shortage designation without first undertaking the notice and comment process required for a rulemaking. ECF 66 at 7-13. Ivim Health will not duplicate Plaintiffs' legal arguments concerning why FDA's decision to label a generally applicable determination with broad public-health impact as an adjudication is contrary to the Administrative Procedure Act. Rather, Ivim Health will focus on how FDA's bypass of notice and comment negatively impacted the quality of its decision-making process by limiting the information available to the public.

Notice and comment is designed to "ensur[e] 'due deliberation' with the important stakeholders," *Texas v. Becerra*, 577 F. Supp. 3d 527, 550 (N.D. Tex. 2021) (quoting *Smiley v. Citibank (S.D.) N.A.*, 517 U.S. 735, 741 (1996), and "to allow the agency to benefit from the expertise and input" of affected parties, *La Union del Pueblo Entero v. Fed. Emergency Mgmt. Agency*, 141 F. Supp. 3d 681, 691 (S.D. Tex. 2015) (quotation marks omitted). "The more

expansive the regulatory reach" of the agency's action, "the greater the necessity for public comment." *Texas*, 577 F. Supp. 3d at 550 (quoting *Am. Fed. Of Gov't Emp., AFL-CIO v. Block*, 665 F.2d 1153, 1156 (D.C. Cir. 1981)).

Here, an open notice and comment process would have involved members of the public, such as patients who are directly impacted by the lack of access to branded tirzepatide, doctors who seek to aid them, and telehealth providers like Ivim Health whose medical providers work directly with patients, offering an opportunity to present FDA with a fuller picture of the reality of their decision. *See, e.g.*, *U.S. Dep't of Labor v. Kast Metals Corp*., 744 F.2d 1145, 1153 n.17 (5th Cir. 1984) (citation omitted) ("Section 553 was enacted to give the public an opportunity to engage in the rule-making process."). In particular, medical providers and institutions like Ivim Health would have been able to provide FDA with information regarding the significant barriers that patients continue to face in gaining access to tirzepatide. This creates significant negative health impacts on patients when access to medical therapy is interrupted. As explained above, p. 10, *supra*, Ivim Health's experience on the ground is that supply of tirzepatide remains restricted and unreliable, with the availability of compounded versions serving as a critical safety valve.

Instead, by foregoing notice and comment and characterizing its proceeding as an adjudication despite the broad public impact, FDA was left to lean heavily on information submitted by Eli Lilly regarding the company's current and projected supply capacity. Decision at 5-16. Of course, information from the manufacturer is relevant to FDA's shortage determination, but it offers far too limited a perspective, including because a manufacturer's incentives on supply capacity may not align with the public interest. *Cf. Am. Rivers v. FERC*, 895 F.3d 32, 50 (D.C. Cir. 2018) (finding agency decision arbitrary in part because no "independent verification" of market participant's assertions was "undertaken"). A publicly traded company like Eli Lilly not only has an interest but

an obligation in maximizing its profits for its shareholders. This provides a strong incentive to box out alternative supply sources without any corresponding objective to ensure adequate supply for the broadest possible patient population. To the contrary, for a company with market power, it will generally maximize profits to limit output and keep prices higher. *See Ohio v. Am. Express Co.*, 585 U.S. 529, 549 (2018) ("Market power is the ability to raise price profitably by restricting output").

To be sure, FDA indicated in its decision that it did receive informal submissions from sources other than Lilly, including some telehealth companies and a handful of individual patients, in addition to pharmacy compounders and their representatives. Decision at 4. FDA ultimately dismissed such submissions as too limited, as it raised various objections to the scope and reliability of the evidence presented, ultimately concluding that they reflected only "intermittent challenges." *Id.* at 2. But FDA's response only underscores why the *ad hoc* process it ran is not a substitute for formal notice and comment. Notice and comment is designed to require an agency "to disclose" *upfront* "its thinking on matters that will affect various stakeholders." *Texas Med. Ass'n v. U.S. Dep't of Health & Hum. Servs.*, 587 F. Supp. 3d 528, 544543 (E.D. Tex. 2022). In doing so, the agency previews where it intends to go while identifying the issues it believes are important and areas where it needs more information, providing a fair opportunity for meaningful response and allowing the public to seek to "influence agency decision making at an early stage, when the agency is more likely to give real consideration to alternative ideas." *U.S. Steel Corp. v. U.S. E.P.A.*, 595 F.2d 207, 214 (5th Cir. 1979); *see also U.S. Dep't of Labor v. Kast Metals Corp.*, 744 F.2d 1145, 1153 n.17 (5th Cir. 1984) ("[Section 553] enables the agency promulgating the rule to educate itself before establishing rules and procedures which have a substantial impact on those who are regulated.").

Put in the context of this case, if FDA had identified in advance the assumptions it was making regarding tirzepatide supply and the type of evidence it would consider, public health

providers like Ivim Health would have been positioned to provide highly relevant information that would have provided FDA with a more complete perspective on an urgent matter of public health.

III. The public interest strongly favors judicial intervention to minimize disruptions to patient access.

A. Removing tirzepatide from the shortage list prematurely would harm the health of patients whose treatments are disrupted.

To the extent that the Court concludes that Plaintiffs have satisfied the first three factors for securing preliminary injunctive relief, Ivim Health respectfully submits that the public interest overwhelmingly favors preserving the status quo and ensuring that access to compounded tirzepatide is maintained while this litigation proceeds. As Plaintiffs have explained, there is significant case law recognizing access to continued healthcare promotes the public interest. *See Natera, Inc. v. NeoGenomics Lab'ys, Inc.*, 106 F.4th 1369, 1383 (Fed. Cir. 2024) (finding a preliminary injunction did not apply to patients who were using a cancer treatment before entry of injunction, as access to the treatment "is vital for their continued care*"); Dumanian v. Schwartz*, No. 19-cv-6771, 2022 WL 2714994, at *15 (N.D. Ill. July 13, 2022) ("access to . . . medical treatments is unquestionably in the public interest"); *see also Med-Cert Home Care, LLC v. Azar*, 365 F. Supp. 3d 742, 758 (N.D. Tex. 2019) (granting injunctive relief because of the public's strong interest in access to healthcare*); Benson v. St. Joseph Reg'l Health Ctr.*, No. 04-cv-04323, 2005 WL 6459109, at *2 (S.D. Tex. Dec. 22, 2005) (noting "the important public interest in open and fair competition for health services"); *Bos. Heart Diagnostics Corp. v. Health Diagnostics Lab'y, Inc.*, 2014 WL 2048436, at *2 (D. Mass. May 16, 2014) (recognizing the "public's interest in having access to medical treatment"); *Washington State Pharmacy Ass'n v. Gregoire*, 2009 WL 1259632, at *1 (W.D. Wash. Mar. 31, 2009) (recognizing that "it is in the public interest to ensure that the plaintiff pharmacies can continue to serve [patients] and that said [patients] have access to needed prescription drugs").

The public interest strongly supports maintaining the status quo here because continued and reliable access to tirzepatide medicines is essential for patients. Even a temporary loss of access would have significant, negative health outcomes for patients, given the importance of continuity of treatment. Several studies have assessed the discontinuation of GLP-1 medications, including both semaglutide and tirzepatide, for weight loss and for diabetes. In all of these studies, patients exhibited significant weight regain, return of metabolic syndrome, and return of cardiovascular disease risk factors. Lifestyle modification is essential in limiting this regression.

For example, in the SURMOUNT-4 clinical trial, after 36 weeks of treatment with tirzepatide, participants experienced an average weight loss of 20.9% body weight. Louis J. Aronne, et al., *Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial*, JAMA 38-48 (Dec. 11, 2023). But those who withdrew medication had a 14% body weight regain after 52 weeks whereas those who continued therapy saw additional weight loss of 5.5% total body weight. *Id.* at 41. In addition to the above study, another study on FDA approved GLP-1 medications show similar results in regard to rapid weight regain upon discontinuation followed by deleterious health impacts related to cardiometabolic syndrome and increased risk of cardiovascular disease. Theodoros Papathanasiou, et al., *Impact of dose-escalation schemes and drug discontinuation on weight loss outcomes with liraglutide 3.0 mg: A model-based approach*, DIABETES, OBESITY AND METABOLISM 969 (Feb. 19, 2020).

Ivim Health's experience treating patients with compounded tirzepatide strongly implies that abruptly removing access to compound tirzepatide will likely have adverse clinical outcomes. In all cases, robust lifestyle modification and continuous support of a healthcare team is required for patients to have a fighting chance of maintaining weight loss and the concurrent health benefits

that accompany it. Abrupt discontinuation does not allow for medical providers to implement such lifestyle modification or create a titration plan to slowly wean patients off their current medication regimen in a controlled fashion. Clinically, providers rarely opt to discontinue medications without a period of dosage reduction due to increased rates of rapid weight regain when discontinuing medication too quickly. Thus, abrupt discontinuation will likely result in rapid weight regain and could reverse the positive benefits of the patient's therapeutic course.

Clinically, discontinuation of semaglutide (also a GLP-1 medication), and tirzepatide lead to similar results. With rapid weight regain comes the return of metabolic syndrome. John P.H. Wilding, et. al., *Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension*, DIABETES, OBESITY AND METABOLISM 1553, 1554 (April 19, 2022). The STEP-1 extension trial showed that patients discontinuing GLP-1 therapy after 68 weeks of treatment saw increases in systolic and diastolic blood pressure back to baseline which negated the positive change that occurred while on treatment. *Id.* Lipid profiles including LDL and triglycerides have been shown to increase, resulting in dyslipidemia. *Id.* Similarly, serum blood glucose levels have been shown to increase resulting in elevated Hemoglobin A1c levels. *Id.* at 1558. In fact, a substantial volume of patients in these studies were shown to revert to a diagnosis of pre-diabetes and diabetes due to these elevated levels. *Id.* at 1557. CRP, or C-reactive protein, a biomarker used to evaluate inflammatory levels, also increases upon GLP-1 discontinuation. *Id.* at 1556. In the absence of time to slowly adjust therapy and implement lifestyle components to prevent weight regain, abrupt discontinuation of GLP-1 therapy by eliminating access to previously available compounded formularies will likely yield even more negative results.

The return of metabolic syndrome in these patients is directly correlated with an elevated risk of cardiovascular disease and chronic illness. *Id.* at 1554. As noted above, prediabetes and

diabetic conditions will result with elevated increases in HbA1c. Positive cardiovascular effects shown in GLP-1 studies, such as reduction of major adverse cardiovascular events (MACE) including a 20% relative risk reduction in heart attack, stroke, and peripheral vascular disease, will be reversed. A. Michael Lincoff, et. al., *Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes*, NEW ENG. J. OF MED. 2221, 2228 (Dec. 14, 2023). These consequences are not only dire for the individual patient but will result in future exorbitant healthcare costs and claims which currently plague American healthcare.

In short, disrupting the status quo by removing tirzepatide from the shortage list will prevent physicians from exercising their medical judgment to meet patient needs with compounded medicines, forcing unrealistically rapid transitions to Lilly's products at a time when access on the ground to these products remains restricted. The negative public health effects from such an abrupt and premature transition counsel in favor of preliminary injunctive relief.

B. Patient safety considerations further support preliminary injunctive relief.

Eli Lilly has argued that continued access to compounded tirzepatide is contrary to the public interest based on the theory that such medicines are not subject to formal FDA approval and supposedly are less safe and effective. ECF 34 at 6. That supposition is contrary to Ivim Health's experience as a healthcare provider, as responsible physicians exercising sound medical judgment recognize the safety and efficacy of compounded medicines.

Lilly's disparaging of compounded medicines is also inconsistent with the strict regulatory regime Congress has established for compounding pharmacies under Section 503B. *See Athenex Inc. v. Azar*, 397 F. Supp. 3d 56, 59 (D.D.C. 2019) ("An outsourcing facility remains exempt from the FDCA's premarket approval requirements and certain labeling and supply-chain requirements, but only if it satisfies eleven statutory criteria."). Under Congress's framework, compounded drugs must be manufactured "at a facility that is subject to specified FDA licensing, reporting, fees, and

inspection requirements," *id.*; 21 U.S.C. §§ 353b(a)(1), (a)(9), (a)(11), 353b(b); having the "ingredients used in the compounding process meet national standards," *Athenex Inc.*, 397 F. Supp. 3d at 59; 21 U.S.C. § 353b(a)(3); FDA has not ruled the drug to be unsafe nor difficult to compound, *id.* §§ 353b(a)(4), (a)(6); the drug is labeled in accordance with statutory requirements, *id.* § 353b(a)(10); the drug will not be sold or transferred by an entity other than the outsourcing facility, *id.* § 353b(a)(8), amongst many other requirements.

The same cannot be said for the unsafe, unregulated counterfeit and "research" products that are easily accessible to consumers for purchase online. Far from promoting patient safety, if access to compounded medicines is prematurely blocked and gaps in patient access remain, there is a significant risk that patients will turn to less safe alternatives, such as research-grade products or counterfeit products. Ivim Health provided a survey to a group of people interested in GLP-1 medications with over 2,900 responses and asked the following question: "If you could not afford your GLP-1 medication, would you consider utilizing a product containing a GLP-1, like semaglutide or tirzepatide, that is available to buy online without the oversight of a medical provider or a medical prescription". Over 85% of respondents reported "Yes" to this question, illustrating the dangers of removing a readily available, safe, regulated medication from the marketplace. The result of patients flocking to such solutions could be disastrous.

Eli Lilly will likely assert their Lilly Direct program provides a solution for these patients and will help to eliminate any access or supply barriers. But this program only offers the two lowest dosages of Zepbound®, 2.5 mg and 5 mg, which reflect an incredibly small subset of patients—less than 10% of the Ivim Health patient population, for context. In the same survey noted above, Ivim Health asked those people surveyed the maximum amount they could afford for their medical weight loss therapy monthly. Only 4.2% of survey respondents responded within a range of $399 or greater.

This range is the starting price for the Lilly Direct program for the 2.5 mg vial of Zepbound®. This, again, highlights the purported fear that patients unable to access medications due to cost will flock to these counterfeit products as a solution to their abrupt loss of access to their medical therapy.

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In conclusion, it would serve the public interest for the Court to ensure patients have access to care through the continued use of compounded tirzepatide while this litigation proceeds rather than subjecting patients and providers to imminent disruptions. Changes to healthcare accessibility typically impact those who are the most vulnerable—individuals in poor health, lacking financial resources, lacking healthcare providers, lacking health literacy and awareness of options, and those in remote geographic regions most susceptible to supply constraints. In evaluating the public interest, Ivim Health urges the Court to consider the interests of these patients who are likely unaware that their medication may be discontinued and that their health may be significantly impacted by a rushed agency decision that did not allow for meaningful public participation. Compounded tirzepatide should remain available due to the current issues within the supply chain and the negative health impact that would result from patients forced to abruptly discontinue therapy. Upon conclusion of the shortage, significant time should be given to healthcare providers to allow for an appropriate transition of patients on to available alternatives or to provide a titration plan wean patients off of the medication while incorporating lifestyle modification, a process which generally takes years to develop.

CONCLUSION

For these reasons, the Court should grant Plaintiffs' motion for a preliminary injunction.

Dated: February 4, 2025

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CERTIFICATE OF SERVICE

I hereby certify that a true and accurate copy of the foregoing document was filed electronically (via CM/ECF) on February 4, 2025.

Dated: February 4, 2025

/s/ María Amelia Calaf
María Amelia Calaf