IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE: GLUCAGON-LIKE PEPTIDE- 1 RECEPTOR AGONISTS (GLP-1-RAS) PRODUCTS LIABILITY LITIGATION	:	**CIVIL ACTION**
THIS DOCUMENT RELATES TO:	:	**MDL No. 3094 24-md-3094**
ALL ACTIONS/ALL CASES	:	

PLAINTIFFS' RESPONSE TO DEFENDANTS' POSITION STATEMENT

I. Response to Defendants' Litigation Overview

Defendants' GLP-1RA drugs and the unprecedented marketing efforts devoted to their sales may have produced a "paradigm shift" in the way obesity and diabetes are treated but that does not change Defendants' legal obligation to warn prescribers of the serious risks of their drugs. Rather, the popularity of Defendants' drugs highlights that obligation as more patients are exposed to the drugs' serious side effects. As discussed below, even years after the drugs' launch, Defendants' labels for these GLP-1RA drugs continue to omit warnings of the serious injuries alleged by Plaintiffs.

The inadequate warnings pose a serious threat because the safety of Defendants' GLP-1RA drugs is far from well established, as Defendants have yet to conduct long-term studies demonstrating safety. To Plaintiffs' knowledge, the longest study examining the safety of GLP-1RAs lasted only 104 weeks.[1] And we know that significant numbers of users discontinue use of the drugs possibly due to injuries, cost, or other factors. In one study of GLP-1RAs, 38.6% of users discontinued use of GLP-1RAs (a significant number by clinical study standards).[2] Plaintiffs expect discovery to illuminate the extent of safety concerns with Defendants' GLP-1RA drugs and whether Defendants responsibly studied their drugs.

Regarding next steps for this litigation, Plaintiffs share the desire to move the litigation forward, but not at the expense of fairness. Plaintiffs support the use of a Plaintiff Fact Sheet ("PFS") and believe each case filed in the MDL with a valid PFS should be eligible to participate in the bellwether discovery process. Plaintiffs oppose any proposal that would result in the premature dismissal of claims, or in the adoption of a single, restrictive test for proving causation.

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[1] Marso, et al., *Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes*, New England Journal of Medicine (Nov. 10, 2016).
[2] Liss, et al., *Treatment Modification After Initiating Second-Line Medication for Type 2 Diabetes*, Am. J. Managed Care (Dec. 2023).

II. Injuries: Causation and Severity

Defendants suggest that causation of injuries be assessed by only a single test, a gastric emptying study, effectively rejecting the differential diagnosis method for assessing causation – the method used by many of Plaintiffs' own physicians in their expert, clinical judgment. Defendants' proposal would render superfluous plaintiffs' medical records, their medical histories, and their doctors' and experts' clinical judgment. Defendants' proposed approach conflicts with Federal Rule of Evidence 702 and current clinical standards and has no place in this litigation.

Using differential diagnosis, a plaintiff's medical expert may identify all potential causes and rule out unlikely causes until only one remains – and this analysis presents no special problem here. Here, most GLP-1RA users do not suffer from hypothyroidism or nervous system diseases (other proposed causes of gastroparesis),[3] and for such plaintiffs, those causes can be ruled out entirely. The association between GLP-1RAs and a plaintiff's gastroparesis can also be probed with questions about dosage and timing of symptom onset. For example, is there a temporal relationship between the onset of gastroparesis and the use of a GLP-1RA? Did the gastroparesis symptoms emerge or intensify as the plaintiff's dose was being ramped up, or, did a reduction in dose result in improvement of symptoms (a "dose-response relationship")? In many cases, a causal relationship between a plaintiff's injury and the GLP-1RAs at issue can be established through eliminating unlikely causes and examining the temporal relationship between GLP-1RA ingestion and the injury at issue.

Defendants also downplay injuries caused by their drugs, claiming, with no authority, that ileus and bowel obstruction typically resolve "in 1 to 3 days."[4] But Defendants are aware that

[3] Def. PS at 7.
[4] Def. PS at 8.

these conditions can be much more severe, including from cases like that of Ozempic-user Sarah Hammons,[5] age 32, who was hospitalized for ***seventeen*** consecutive days for stomach paralysis and intestinal obstruction, causing severe stomach cramping, vomiting, nausea, and dehydration.

III. Defendants Did Not Adequately Warn Of The Injuries At Issue In This MDL.

Both Novo and Lilly claim in their Position Statements that their GLP-1RA labels warn of the injuries alleged in this case, such as gastroparesis and ileus. But that is inaccurate. In the warning section of a label (governed by specific FDA regulations), the mere reference to potential general gastrointestinal symptoms is insufficient to warn of the risks of the potential severity and longevity of gastroparesis, ileus, and intestinal blockage to which GLP-1RA users are exposed.

A prescription drug label's Warnings and Precautions "must include a concise summary of the most clinically significant safety concerns from the [label] that affect decisions about whether to prescribe the drug, recommendations for patient monitoring to ensure safe use of the drug, and measures that can be taken to prevent or mitigate harm."[6] It must also contain complete information "identif[ying] the risk, its consequences, and recommendations for the clinician to prevent or mitigate it, as appropriate," rather than "[a]mbiguous and uninformative information."[7]

Defendants' labels fall short of these standards for Warnings and Precautions. The labels' reference to common reactions like nausea, vomiting and abdominal pain does not inform prescribers that these symptoms may be signs of life-threatening digestive dysfunction necessitating critical medical care. The labels downplay the symptoms by stating that "the

[5] *Complaint* (Dec. 15, 2023), 2:213-cv-04965 (E.D. Pa.).
[6] FDA, *Guidance for Industry: Labeling for Human Prescription Drug and Biological Products – Implementing the PLR Content and Format Requirements* at 17 (Feb. 2013), at 13 (citing 21 C.F.R. § 201.57(a)(10)), *available at* https://www.fda.gov/media/71836/download (last visited Apr. 11, 2024).
[7] *Id.*

majority of reports of nausea [and] vomiting ... decreased over time,"[8] minimizing these symptoms and denying prescribers and patients the opportunity to make an informed decision.[9] Lilly's warning about "gastrointestinal adverse reactions, sometimes severe" is likewise inadequate and vague: warning of an episode of severe vomiting does not, itself, warn of the risk of weeks of vomiting due to stomach paralysis, which may lead to hospitalization or death, and which may not abate after stopping the drug.

Similarly, a passing reference to "ileus" in the Post-marketing Events section of a label (distinct from the Warnings section) does not help prescribers identify, understand, or mitigate the risk. As Defendants acknowledge, the additional reference to ileus was spurred by an FDA-initiated review, but Defendants should not have waited for the FDA to act. Manufacturers—not the FDA—are responsible for the labeling of their drugs at all times, *Wyeth v. Levine,* 555 U.S. 555, 579 (2009), and manufacturers may not rely on the FDA to promptly ensure the adequacy of drug labeling. *Id.* at 578-79, n. 11. Accordingly, as with a warning for gastroparesis, Defendants could have and should have warned of the risk of ileus in the labeling submitted for initial approval[10] and strengthened the warnings in revised labeling through the CBE process.[11]

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[8] *See, e.g.,* Mounjaro Label at 6 (revised July 2023), *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215866Orig1s002s006lbl.pdf (last visited 4/11/24).

[9] Further, the listing of gastrointestinal symptoms does not warn that those symptoms can persist after cessation of the drugs. *See* Kalas, *et al., Medication-Induced Gastroparesis: A Case Report*, J. INVESTIG. MED. HIGH IMPACT CASE REP. (Jan.-Dec.2021) (case report of patient who experienced nausea, vomiting, and bloating for weeks after discontinuing Trulicity), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8529310/ (last visited Sept.26, 2023); C.T. Jones, *Ozempic Users Report Stomach Paralysis from Weight Loss Drug: 'So Much Hell"*, ROLLING STONE (July 25, 2023) (describing patient who experienced severe nausea both during and after she discontinued use of a GLP-1RA), *available at* https://www.rollingstone.com/culture/culture-news/ozempic-stomach-paralysis-weight-loss-side-effects-1234794601 (last visited 9/26/23).

[10] *In re Actos,* 2014 WL 60298, at *7 (W.D. La. Jan. 7, 2014) ("[D]efendants [can] implement stronger warning language into labeling[] by submitting stronger warning language for FDA approval…"); *see also Anderson v. Merck*, 2022 WL 17096157, at *6 (N.D. Cal. Nov. 21, 2022); *Stube v. Pfizer*, 446 F. Supp. 3d 424, 437 (W.D. Ark. 2020).

[11] *Merck v. Albrecht*, 139 S. Ct. 1668,1673 (2019) (Under the Changes Being Effected (CBE) regulation, manufacturers must "change a label without prior FDA approval… where there is 'newly acquired information' about the 'evidence of a causal association' between the drug and a risk of harm." (citing 21 C.F.R. § 314.70(c)(6)(iii)(A))). Definitive causation need not be shown; only reasonable evidence of a causal association is required. *See Levine*, 555 U.S. at 571 (citing 21 C.F.R. §§ 201.80(e), 314.80(b); 73 Fed. Reg. 49605).

Development of a full factual record is necessary for any evaluation of whether Defendants have sufficiently informed prescribers and patients of "the most clinically significant safety concerns," such as gastroparesis and ileus.

Contrary to Defendants' assertions, they are not entitled to a blanket ruling on preemption that the warnings in their GLP-1RA labels were adequate,[12] and Plaintiffs' claims *do not* arise merely from nausea, vomiting, or constipation. Rather, Plaintiffs' claimed injuries are prolonged, life-threatening digestive dysfunction of which Defendants have never warned. As the Western District of Louisiana held, even with Ozempic's reference to delayed gastric emptying in the Mechanism of Action and Drug Interaction sections of the label and its listing of "gastrointestinal conditions such as 'nausea, vomiting, diarrhea, abdominal pain, and constipation'" as potential adverse events, Plaintiff Jaclyn Bjorklund set forth "a plausible claim for relief" regarding Novo's failure to warn about gastroparesis.[13] Similarly, the court held that, due to "growing awareness" of gastroparesis as an adverse effect of GLP-1RA use, Bjorklund adequately alleged that Lilly should have added a warning about gastroparesis to the Mounjaro label.[14]

IV. Any Preliminary Roadmap Must Be Fair.

Plaintiffs support moving the litigation forward but oppose Defendants' proposal to dispose of cases before any meaningful opportunity for discovery. Discovery is essential to a full and fair adjudication of the merits of plaintiffs' individual claims. This MDL should "provid[e] a

[12] For that argument, Defendants cite *In re Taxotere*, 462 F. Supp. 3d 650 (E.D. La. 2020), an inapposite summary judgment ruling. Even in *Taxotere*, the court's ruling on the adequacy of Taxotere's warning as a matter of law applied only to the revised label after a warning was added. *Id.* at 653.
[13] *Bjorklund v. Novo Nordisk A/S*, 2023 WL 8528445, at *3 (W.D. La. Dec. 8, 2023); *Breaux v. Novo Nordisk Inc.*, 2023 WL 8606799, at *3 (W.D. La. Dec. 12, 2023) (same).
[14] *Bjorklund v. Novo Nordisk, A/S*, 2023 WL 8584961, at *4 (W.D. La. Dec. 11, 2023).

forum for all parties to have a fair test of the merits of their claims and defenses; … [and] effect[] the statutory and common-law goals of compensating those injured by tortious conduct[.]"[15]

Defendants' contention that PFS responses will enable early disposition overlooks the need for individual fact and state-law inquiries, and expert opinion. Again, Defendants' suggestion that plaintiffs must have a gastric emptying studying to prove their gastroparesis injuries is flawed: Gastric emptying test results may be inconclusive, unavailable, and, depending on an expert's clinical judgment, unnecessary to prove injury.

Moreover, Defendants' suggestion of using data points in the PFS for an accelerated quasi-summary judgment process on issues such as causation and statute of limitations invites oversimplification and runs contrary to the Federal Rules of Civil Procedure. Such issues are almost always fact-intensive, contextual, or the subject of expert opinion. For example, Defendants oversimplify the causation analysis by failing to acknowledge that, under applicable state laws, Defendants' drugs need not be the sole cause of a plaintiff's injuries. Instead, plaintiffs can establish causation by demonstrating through expert opinion that Defendants' GLP-1RA drugs were a "substantial contributing factor" to their injuries. The PFS process is important for providing information relevant to those issues and others, but it is not, itself, a fair and adequate way to fully adjudicate or dispose of claims on the merits. The bellwether process and other discovery will be necessary to test the sufficiency of most plaintiffs' cases, and with rare exceptions, plaintiffs' cases will not be subject to dismissal or early summary judgment based upon their PFS alone.

Instead, the PFS process serves the valuable function of informing the bellwether process, which has significant advantages to both sides. Bellwether cases enable parties to evaluate the

[15] David F. Herr, MANUAL FOR COMPLEX LITIGATION, FOURTH, at §22.2 (2017); *see also* Fed. R. Civ. P. 1.

claims asserted, including questions of causation and liability, and for claims to be weeded out in line with test case rulings to facilitate resolution on a larger scale. A bellwether process will allow the parties to set value on pending claims, potentially dismiss claims *on the merits* without repetitive motion practice and allow for a swift and inexpensive adjudication. Cases with valid PFSs that are not selected for an early bellwether trial should be held until after the bellwether process, when their PFSs can inform decisions about resolution, remand, or further discovery. [16]

[16] *Supra* n. 15 at §22.314 ("The judge also might consider setting several individual cases on a schedule for pretrial motions, discovery, and trial as test cases, while holding other cases or claims in abeyance.").

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Respectfully submitted,

/s/ Parvin K. Aminolroaya
Parvin K. Aminolroaya
SEEGER WEISS LLP
55 Challenger Rd., 6th Floor
Ridgefield Park, NJ 07660
Telephone: (973) 639-9011
Email:paminolroaya@seegerweiss.com

/s/ Jonathan D. Orent
Jonathan D. Orent
MOTLEY RICE LLC
40 Westminster Street., 5th Floor
Providence, RI 02903
Telephone: (401) 457-7700
Email: jorent@motleyrice.com

/s/ Paul Pennock
Paul Pennock
MORGAN & MORGAN
350 Fifth Avenue, Suite 6705
New York, NY 10118
Telephone: (212) 738-6299
Email: ppennock@forthepeople.com

/s/ Sarah Ruane
Sarah Ruane
WAGSTAFF & CARTMELL
Kansas City, MO 64112
Telephone: (816) 701-1123
Email: sruane@wcllp.com