No. _____

IN THE
Supreme Court of the United States

BIOGEN MA INC.,

Petitioner,

v.

EMD SERONO, INC., PFIZER INC.,

Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

PETITION FOR A WRIT OF CERTIORARI

NICHOLAS GROOMBRIDGE
ERIC ALAN STONE
PETER SANDEL
JENNY C. WU
JOSEPHINE YOUNG
PAUL, WEISS, RIFKIND WHARTON & GARRISON LLP
1285 Ave. of the Americas
New York, NY 10019
(212) 373-3000

JEFFREY A. LAMKEN
Counsel of Record
MOLOLAMKEN LLP
The Watergate, Suite 500
600 New Hampshire Ave., N.W.
Washington, D.C. 20037
(202) 556-2000
jlamken@mololamken.com

Counsel for Petitioner

QUESTION PRESENTED

The patent in this case claims a method of medical treatment that requires use of a "recombinant," or synthetic version, of a human protein. That synthetic, recombinant version does not exist in nature. The Federal Circuit held, in violation of this Court's longstanding precedent, that the claim term "recombinant" must be ignored in assessing whether the method of treatment is novel. The question presented is:

Whether courts may disregard the express claim term "recombinant" so as to render a method-of-treatment patent anticipated—and thus invalid—in light of prior-art treatments that used the naturally occurring human protein, where it is undisputed that the recombinant protein was not used in the prior art?

PARTIES TO THE PROCEEDINGS

Petitioner is Biogen MA Inc. ("Biogen"). Respondents are EMD Serono Inc. and Pfizer Inc. (together except where noted, "Serono").

Bayer Healthcare Pharmaceuticals, Inc. and Novartis Pharmaceuticals Corp. (together except where noted, "Bayer") were defendants in a parallel district court proceeding, previously consolidated with this case but later severed, at Bayer's request.

CORPORATE DISCLOSURE STATEMENT

Pursuant to Rule 29.6 of the Rules of this Court, Petitioner Biogen MA Inc. states that it is a wholly owned subsidiary of Biogen Inc., which is a publicly held corporation traded on the Nasdaq Stock Market under the symbol BIIB. No other publicly held corporation owns 10% or more of the stock in Biogen MA Inc.

TABLE OF CONTENTS

TABLE OF CONTENTS—Continued

TABLE OF AUTHORITIES

Page(s)

CASES

STATUTES AND RULES

TABLE OF AUTHORITIES—Continued

TABLE OF AUTHORITIES—Continued

TABLE OF AUTHORITIES—Continued

TABLE OF AUTHORITIES—Continued

IN THE

Supreme Court of the United States

BIOGEN MA INC.,

Petitioner,

v.

EMD SERONO, INC., PFIZER INC.,

Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

---

PETITION FOR A WRIT OF CERTIORARI

OPINIONS BELOW

The opinion of the Federal Circuit is reported at 976 F.3d 1326 and reproduced at App., *infra*, 1a-21a. The opinion of the district court is reported at 335 F. Supp. 3d 688 and reproduced at App., *infra*, 46a-155a.

STATEMENT OF JURISDICTION

The Federal Circuit entered judgment on September 28, 2020, App., *infra*, 1a, and denied rehearing and rehearing en banc on December 18, 2020, App., *infra*, 157a. This petition is timely pursuant to this Court's Rule 13 and this Court's March 19, 2020 Order. The Court has jurisdiction under 28 U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED

The relevant provision of Title 35 of the United States Code is reproduced at App., *infra*, 158a-159a. Section 102 of Title 35, as applicable to pre-America Invents Act ("pre-AIA") patents such as the patent here, states in relevant part:

> A person shall be entitled to a patent unless–
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States.

35 U.S.C. § 102(a)-(b) (2006).

PRELIMINARY STATEMENT

The Federal Circuit's decision in this case upends decades of settled jurisprudence that the invention of a new medical treatment is patentable. The decision holds that a novel, never-performed method of treating disease can be anticipated—*i.e.*, deemed not new and thus unpatentable—even though the claimed method had never been disclosed or performed in the prior art.

Here, the claimed method of treatment required the use of "recombinant" or genetically engineered biological material that was different from the naturally occurring human protein. The prior art did not disclose such treatment. The art did disclose treatment methods using the

analogue human protein, but such treatments were unworkable because the naturally occurring protein could not be harvested in sufficient quantities. Yet the Federal Circuit held the patent's requirement of administering a structurally different "recombinant" protein could simply be ignored. As a result, it ruled that an old and unworkable treatment method using the natural protein could anticipate and invalidate the claim to a novel and new method that has transformed medicine.

If not corrected, the decision will have severe adverse consequences for biomedical research and development. Recombinant therapies have enormous medical significance. More than 140 recombinant proteins have been approved for therapeutic use by the Food and Drug Administration, and five of the top ten therapeutic products by sales value are recombinant proteins. Analysts estimate the annual global market for recombinant therapeutics to be over $90 billion. Many diseases and conditions are caused by the human body failing to make, or failing to make enough of, a given human protein. Methods of treatment using proteins made with recombinant techniques allow scientists and pharmaceutical innovators to replace or augment those human proteins with recombinant analogues. Across the medical landscape, from hemophilia to diabetes to cancer to multiple sclerosis, methods of treatment with recombinant proteins have revolutionized patient care for millions and millions of patients. For example, there are more than one million patients suffering from multiple sclerosis in this country; before recombinant interferon-β there was no treatment available. Approximately six million Americans take recombinant insulin. Across the spectrum of diseases, millions of lives have been improved or saved with these therapies.

Those inventions, however, are highly expensive and risky. The most recent studies show that bringing a new biologic medicine (the category in which recombinant proteins fall) to market costs $2.6 billion on average. For every successful new treatment, there can be dozens of failures. See, *e.g.*, Biotechnology Innovation Organization, *Clinical Development Success Rates 2006-2015*, at 3 (2016).[1] Robust patent protection allows the United States to maintain its position as the world's leading biomedical innovator. The Federal Circuit's decision imperils the scientific investments needed to develop these promising new therapies that may help millions of patients. Personalized medicine is now moving to the fore and recombinant technology is becoming ever more important. The timing of the Federal Circuit's sea change could not be worse.

This case concerns an invention that dates from the dawn of—and that helped prompt—the biotechnology revolution. In 1980, when today's techniques for producing new biological products were mere hypotheses, scientist Walter Fiers did something unprecedented: He caused E. coli bacteria to produce an analogue to a protein ordinarily generated by the *human immune system*—interferon-β. He determined, moreover, that the interferon-β he was able to produce in bacteria matched the biological activity of the native, human protein.

Dr. Fiers thus solved a problem that had plagued science (and fascinated the popular press) for years. Human interferon-β was thought to be a treatment for all manner of viral conditions and diseases. It was, however,

---

[1] https://www.bio.org/sites/default/files/legacy/bioorg/docs/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf.

available in only infinitesimally small amounts, harvested with great difficulty from discarded human tissue. Dr. Fiers overcame this problem using "recombinant" DNA technology. That technology takes genetic material from different sources and joins them—or "recombines" them—before inserting them into a host cell. The host cell—in this case, a *non-human* host cell—in turn uses the DNA to produce a synthetic protein having similar properties but a different molecular structure from the human protein. By producing recombinant interferon-β in a non-human cell, and proving that it had the same biological activity as the naturally occurring human version, Dr. Fiers overcame a barrier—scarcity—that had prevented that protein's widespread medical use. Biogen, which underwrote Dr. Fiers's research, made the financial investments needed to turn that discovery into Avonex®, a leading treatment for multiple sclerosis.

Dr. Fiers's patent application spent 29 years being thoroughly examined by the Patent Office.[2] By the time the patent issued in 2009 as U.S. Patent No. 7,588,755 (the "'755 Patent"), respondents EMD Serono, Inc. and Pfizer Inc. together sold their recombinant interferon-β product Rebif® for use in a treatment that the jury found infringes Biogen's patent. Following trial and verdict, the district court entered judgment for Biogen. It rejected as a matter of law respondents' argument that treatments using naturally occurring human interferon-β anticipate treatments using recombinant interferon-β. App., *infra*, 55a-81a. Under longstanding precedent,

---

[2] Much of that time was consumed by interference proceedings to determine who was the first inventor of the subject matter, as several applicants had filed for patents. Substantive review was suspended—in effect, stayed—for a lengthy period because of actual or potential interferences.

proof of anticipation requires the defendant to establish that each and every element of the patent claim was disclosed in a single prior art reference. "The evidence presented at trial," the court explained, "demonstrates that native interferon-β and recombinant interferon-β are not structurally identical," App., *infra*, 65a, and thus prior art methods using native interferon-β could not anticipate Dr. Fiers's patented method.

The Federal Circuit's decision reversing that judgment does violence to this Court's precedents and threatens the viability of patent protection for—and thus the incentive to develop—treatments using recombinant technologies. It invoked "product-by-process law," under which an old product does not become patentable merely because it is made by a new process. App., *infra*, 12a-17a. That law, it ruled, applies to and invalidates the '755 Patent's method-of-treatment claims because the same treatment using natural (not recombinant) interferon-β was previously known. App., *infra*, 17a-20a. That holding runs headlong into this Court's decision in *Association for Molecular Pathology* v. *Myriad Genetics, Inc.*, 569 U.S. 576, 595 (2013), which recognizes that methods of treatment are patentably distinct from the products administered in those methods. In *Myriad*, this Court held that, although the DNA coding for a human protein could not be patented, methods of treatment based on that protein were analytically distinct: "It is important to note what is *not* implicated by this decision. First, there are no method claims before this Court. Had Myriad created an innovative method of manipulating genes while searching for the BRCA1 and BRCA2 genes, it could possibly have sought a method patent." *Id.* at 595.

Rejecting that very distinction here, the Federal Circuit held that the '755 Patent's method of treatment

using recombinant interferon-β was anticipated even though that method did not exist in the prior art. It further ignored that recombinant interferon-β made in a non-human cell is not identical to native, human interferon-β. That was error. And it rejected the district court's exercise of its discretion to grant a new trial, holding such method-of-treatment claims invalid as a matter of law even though, all agree, the method had never before been practiced.

The Federal Circuit's ruling does not merely negate an unbroken line of cases stretching back to before the Patent Act. It threatens innovation where it is needed most: to cure diseases against which the body's natural immune response is insufficiently robust. This Court should grant review, reverse the Federal Circuit, and either reinstate the district court's judgment as a matter of law of no anticipation or reinstate its conditional grant of a new trial on that issue.

STATEMENT OF THE CASE

This case concerns the sort of breakthrough that the patent laws unquestionably should reward. The '755 Patent is directed to a treatment that was not previously possible—administering a new recombinant protein that has the biological activity of naturally occurring interferon-β. Recombinant interferon-β was the first successful large-scale therapy for multiple sclerosis, a devastating disease in which the body's own immune mechanism damages the material that insulates and protects the nerves.

I. Technological Background Of The Invention And The Resulting Patent

A. The Unfulfilled Promise of Interferon-β, and Dr. Fiers's Solution

The human immune system makes proteins called "interferons" to help fend off attacks by viruses. See, *e.g.*, C.A. App. 7783 (24:30-18). Beginning in the 1950s, doctors sought to isolate human interferons and to use them to treat viral diseases, cancers, and other conditions. C.A. App. 118-119 (2:53-4:22); C.A. App. 7784 (25:13-23). By the late 1970s, one form of human interferon, interferon-β, had shown great promise as a miracle drug. See C.A. App. 66140. But interferon-β is found in only infinitesimal amounts in human cells. C.A. App. 119 (4:49-55). The most common source of interferon-β was fibroblast cells in discarded human foreskin. See C.A. App. 119-120 (4:49-5:3). Harvesting interferon-β from those cells was inefficient and yielded impure compositions. *Ibid.* Thus, in 1979, *Omni* described interferons as the "miracle cure at $22 billion per pound." C.A. App. 66140. The next year, *Time* dubbed interferons "the IF drug," playing on their name and their tantalizing unobtainability. C.A. App. 66145-66146.

1. As the '755 Patent (with a priority date of June 6, 1980) explained, human interferon "has potential application in antitumor and anticancer therapy," but such "applications of IFN-β have been severely hampered by lack of an adequate supply of purified IFN-β." C.A. App. 119 (3:57-4:13). Dr. Fiers noted that then-"recent advances in molecular biology" created the possibility for recombinant expression of desired proteins in non-human cells. C.A. App. 120 (5:4-16). He achieved that goal, producing interferon-β with the "immunological or biological activity of" human interferon-β. C.A. App. 120 (5:49-6:5).

"By virtue of this invention," he explained, "it is possible to obtain polypeptides displaying an immunological or biological activity of" human interferon-β "for use in antiviral, antitumor or anticancer agents and methods. This invention allows the production of these polypeptides in amounts and by methods hitherto not available." C.A. App. 120 (5:54-59).

Dr. Fiers was not the only person working to achieve that goal. Several groups of the world's leading scientists were attempting to express interferon-β in a non-human cell line and to determine whether the resulting, recombinant protein would have biological activity like that of native, human interferon-β. But Dr. Fiers was the first to figure out how to achieve that goal. He was the first to recombinantly express interferon-β-like proteins and to demonstrate that, even though they are structurally different from the human analogue, they have the biological and immunological activity of native, human interferon-β. Because recombinant proteins can be *manufactured* in large quantities, this meant they could be made in therapeutically effective amounts for treatment. See C.A. App. 136-140 (37:18-46:37). The United States Patent Office awarded Dr. Fiers the '755 Patent, directed to methods of treatment using *recombinant* interferon-β made in a non-human cell.

2. While the recombinant interferon-β mimics the activity of native human interferon, it is not structurally identical to naturally occurring human interferon-β. Like all proteins (or "polypeptides"), interferon-β consists of amino-acid building blocks. C.A. App. 77878 (29:2-13). Specifically, interferon-β comprises 166 amino acids connected end-to-end. C.A. App. 77878 (29:19-22). Because of various molecular forces, that linear array of amino acids will conform or fold into a complex three-dimen-

sional shape. If the three-dimensional shape is correct, interferon-β will be biologically active, C.A. App. 77880 (31:8-14), modulating the immune system, reducing inflammation, and increasing cells' resistance to viruses. C.A. App. 77574 (62:2-9); C.A. App. 77872 (23:15-19); C.A. App. 47551 (47:14-15). In effect, the complex three-dimensional shape is like a key, fitting into a lock to set in motion subsequent biological processes.

Native, human interferon-β is a glycoprotein, which means it has sugars attached to one of its amino acids in a branched structure. C.A. App. 77882 (33:11-25). The sugar branches can vary for individual interferon-β proteins, even when they are made within the same cell. Thus, in any given sample of native interferon-β taken from a human, each interferon-β molecule can have one of a variety of sugar branches attached to it. C.A. App. 51646 (Kagawa); C.A. App. 80514-80515 (100:5-101:2).

While *similar* proteins can be made by cells of different species, the cells of different species make glycoproteins with different sugar branches, or sometimes none at all, and are thus not identical. E. coli, for example, does not glycosylate proteins. C.A. App. 80514 (100:5-20); C.A. App. 79094 (47:12-21). The interferon-β-like proteins produced by E. coli thus lack the sugar attachments of native, human interferon-β and thus have a different molecular structure.

B. The '755 Patent

The '755 Patent discloses that therapeutic use of native, human interferon-β was known in the prior art, C.A. App. 118-110 (2:53-4:22), and how compositions of native, human interferon-β had been prepared, C.A. App. 119-120 (4:49-5:3). Its claims were limited to a method of treatment with "a therapeutically effective amount of a

composition," said composition comprising a *recombinant* interferon-β-like polypeptide made in a *non-human host* transformed by certain DNA sequences.

During prosecution of a sister patent application, Biogen explained that the "non-human" host limitation was added for the purpose of distinguishing recombinant interferon-β from native interferon-β:

> As amended, the claims expressly recite production in non-human cells. * * * This is not semantics. IFN-β produced in human cells is glycosylated and has a particular type and content of sugar groups. The claimed polypeptides do not have the identical type or content of sugar groups. They cannot have. They are produced in non-human cells whose ability to post-translationally modify proteins is different from that of human cells.

C.A. App. 24315.

Claim 1 of the '755 Patent thus recites:

> 1. A method for immunomodulation or treating a viral condition[ ], a viral disease, cancers or tumors comprising the step of administering to a patient in need of such treatment a therapeutically effective amount of a composition comprising:
>
> a *recombinant* polypeptide produced by a *non-human* host transformed by a recombinant DNA molecule comprising a DNA sequence selected from the group consisting of:
>
> (a) DNA sequences which are capable of hybridizing to any of the DNA inserts of G-pBR322(Pst)/HFIF1, G-pBR322(Pst)/HFIF3 (DSM 1791), G-pBR322(Pst)/HFIF6 (DSM 1792), and G-pBR322 (Pst)/HFIF7 (DSM 1793) under hybridizing condi-

> tions of 0.75 M NaCl at 68° C. and washing conditions of 0.3 M NaCl at 68° C., and which code for a polypeptide displaying antiviral activity, and
>
> (b) DNA sequences which are degenerate as a result of the genetic code to the DNA sequences defined in (a);
>
> said DNA sequence being operatively linked to an expression control sequence in the recombinant DNA molecule.

App., *infra*, 4a-5a (emphasis added); see C.A. App. 142 (49:59-50:12).

II. Proceedings Below

In 2010, Biogen sued respondents for infringement of claims 1 and 2 of the '755 Patent.

A. Proceedings Before the Trial Court

1. During a nearly five-week trial, the jury heard about worldwide efforts in 1980 among leading scientists to do what had never been done: to use recombinant-DNA technology to engineer an analogue of a known human protein, interferon-β, that had biological activity like the native, human protein and that thus could be used to treat disease. Pet'r C.A. Br. 2. The jury heard that Dr. Fiers produced interferon-β-like polypeptides in E. coli, rigorously tested and retested their biological activity to exclude false positives, and filed his patent application before anyone else. *Ibid.* The jury heard extensive testimony about the patent's 29-year history in the Patent Office (during much of which time prosecution was suspended due to multiple interference proceedings). And the jury heard respondents' refrain, which the jury rejected, that all this was obvious. *Id.* at 3.

What the jury did not hear was any evidence that the '755 Patent was anticipated by the prior art. Pet'r C.A. Br. 15-16. No witness identified a prior-art reference in which recombinant interferon-β, made in a non-human host cell, was used to treat disease. Indeed, everyone agreed that had never happened. *Ibid.* Nor did any witness testify that recombinant interferon-β and native, human interferon-β are themselves identical. *Id.* at 23. Indeed, respondents' expert conceded that they are not identical. *Ibid.* When it came time for summations, respondents did not even mention their anticipation defense. *Id.* at 31. Consistent with this Court's precedents—and without objection—the district court instructed the jury that it must compare the claimed method of treatment to the prior art to determine whether the "identical invention" was made, used, or disclosed before. C.A. App. 47665.

The jury found that the use of respondents' recombinant interferon-β product, Rebif®, directly infringes claims 1 and 2 of the '755 Patent, and that respondents Serono and Pfizer each contribute to the infringement under 35 U.S.C. §271(c). Pet'r C.A. Br. 10. The jury rejected respondents' obviousness, written-description, and enablement defenses.[3] *Ibid.* The jury found, however, that the claims of the '755 Patent are anticipated by prior-art uses of native, human interferon-β. *Ibid.*

2. All parties sought judgment as a matter of law. The district court's "comprehensive opinion," App., *infra*, 7a—spanning over 90 pages, App., *infra*, 46a-154a—care-

[3] While not relevant to this petition, the jury found in favor of respondents on induced infringement under 35 U.S.C. §271(b), App., *infra*, 83a, a ruling the district court then overturned as a matter of law, *id.* at 84a-96a.

fully reviewed the evidence before the jury. App., *infra*, 62a-74a. It denied respondents' motions across the board, App., *infra*, 154a, and it granted Biogen's motions to set aside the verdict on anticipation. It held that product-by-process law does not render the patent anticipated. That law, it explained, does not apply to a method of treatment that uses a product made in a particular way. App., *infra*, 77a-81a. It held that the products used in the treatment were not identical to native interferon-β in any event. App., *infra*, 65a-77a. Among other things, native interferon-β is glycolsylated—that is, it has sugar branches attached to one of its amino acids. Recombinant interferon-β made in a non-human cell, on the other hand, has different glycolsylation patterns, or, in the case of recombinant interferon-β made in E. coli, no glycosylation at all. App., *infra*, 66a-72a.

Because the anticipation defense had received scant attention at trial, the district court also exercised its discretion to conditionally grant a new trial on anticipation under Fed. R. Civ. P. 50(c). App., *infra*, 81a-82a. The court found that the jury's determination was "against the weight of the evidence" and that a new trial was warranted because of "the overall setting of the trial, the character of the evidence, and the complexity of the legal principles that the jury was asked to apply to the facts." App., *infra*, 82a. As the district court explained, the jury spent the vast majority of the five-week trial hearing testimony on issues other than anticipation. *Ibid.* Because the "five-week trial in this case was 'long and complicated,' required complex factual determinations on multiple infringement, validity, and damages issues, was noticeably focused on issues other than anticipation, and involved scientific concepts that are not the 'subject matter . . . lying within the ordinary knowledge of jurors,'" a

new trial would be warranted if its ruling in favor of Biogen were overturned on appeal. App., *infra*, 81a (quoting *Lind* v. *Schenley Indus., Inc.*, 278 F.2d 79, 90-91 (3d Cir. 1960)). Because a judgment in a patent case leaving open only damages issues is immediately appealable as of right, see 28 U.S.C. §1292(c)(2), respondents appealed.

B. The Federal Circuit's Decision

The Federal Circuit reversed the district court's grant of judgment as a matter of law, reinstated the jury's verdict of anticipation, and held that the district court had abused its discretion in conditionally granting a new trial.

The Federal Circuit noted the longstanding rule that a claim is anticipated "only if 'each and every [limitation] is found within a single prior art reference.'" App., *infra*, 10a (citing *Summit 6, LLC* v. *Samsung Elecs. Co.*, 802 F.3d 1283, 1294 (Fed. Cir. 2015)). It then proceeded to jettison that rule. The claims at issue claimed treatment of disease with a *recombinant* polypeptide made *in a non-human host cell*, something that respondents conceded did not exist in the prior art. Indeed, as the district court explained, the use of recombinant interferon-β is what overcame the biggest obstacle in the prior art—the difficulty of obtaining interferon-β in sufficient quantities. App., *infra*, 80a.

The Federal Circuit nevertheless applied product-by-process case law to make the novelty of the claimed method of treatment irrelevant. App., *infra*, 12a-14a. Under that case law, parties cannot claim an existing *product* made by a new *process*; the pre-existing product anticipates a claim to the same product regardless. App., *infra*, 12a-13a. Here, the Federal Circuit expanded this

concept into method of treatment claims, holding that anticipation by the prior method of treatment cannot be avoided based on the "recombinant origin of the recited composition." App., *infra*, 13a-14a.

Although the product-by-process rule by its terms prevents parties from asserting claims to an existing composition—a product—based on the process used to make it, the Federal Circuit held that it applies to method-of-treatment claims like this one. App., *infra*, 14a. The only thing that matters, the court stated, is whether the composition recited in the patent claim is identical to one previously identified in the art—here, whether recombinant interferon-β itself is identical to (and thus anticipated by) the native, human protein. App., *infra*, 15a-16a; see App., *infra*, 14a (the question is "whether the recombinant *product* is identical to the prior art *product*").

The Federal Circuit then ignored the undisputed evidence that recombinant interferon-β made in a non-human cell and native, human interferon-β are *not* the identical product. App., *infra*, 17a-20a; see *Amgen Inc.* v. *Hoffman-La Roche Ltd.*, 580 F.3d 1340, 1366-67 (Fed. Cir. 2009). Instead, it looked only at the identity and sequence of amino acids, ignoring other structural differences in the rest of the molecule. App., *infra*, 17a. As discussed above, the amino acids in a polypeptide make up only part of its structure. Because the amino acid sequences are the same in the recombinant and native proteins, the Federal Circuit held that methods of treatment with recombinant interferon-β made in a non-human cell are anticipated by prior-art treatments with the non-identical human protein. App., *infra*, 18a-20a. For similar reasons, it overturned the district court's conditional grant of a new trial, holding the claims here

anticipated as a matter of law. App., *infra*, 21a. In short, the Federal Circuit held that Dr. Fiers's use of recombinant technology to create a new way to treat disease was unpatentable because, in the Federal Circuit's mistaken view, Dr. Fiers's claimed method was no different from the prior method he had sought to improve.

REASONS FOR GRANTING THE PETITION

The Federal Circuit's decision contravenes this Court's precedents. In doing so, it needlessly threatens to preclude patent protection for—and thereby destroy the incentive to invent—life-saving and life-altering treatments using recombinant technologies. That outcome should not be approved, and especially should not be countenanced now. Personalized medicine, driven by the use of recombinant technology, holds the promise of better, safer, less painful treatments for previously incurable diseases. The Federal Circuit's decision threatens to render those treatments unpatentable, removing an important incentive to develop them and undermining the purpose of the patent system. The issue is important, recurring, and squarely presented. Review is warranted.

I. THE FEDERAL CIRCUIT'S DECISION CONTRAVENES THIS COURT'S SETTLED PRECEDENTS

The '755 Patent claims methods of treatment with a "*recombinant polypeptide* produced by a *non-human host*" that has the amino-acid sequence of native, human interferon-β. Everyone—Biogen, respondents, and the Federal Circuit—agrees that there were no such treatments in the prior art. Before Dr. Fiers's invention, recombinant interferon-β did not exist and thus had never been used in treating disease. The purpose of the worldwide scientific effort in which he participated—and in which he prevailed—was to produce therapeutically

viable amounts of an analogue to human interferon-β in non-human cell lines; native, human interferon-β could not be harvested in sufficient amounts to treat disease. The Federal Circuit has now held that the winner of the global race to find this new method of treatment should have been denied a patent because, in its view, one cannot patent methods of treatment with a recombinantly made version of a human protein, despite their structural differences, and despite the fact that no method of treatment using that recombinant protein existed in the prior art. That holding imperils the development of treatments for all manner of diseases. It also trenches on decades of law from this Court.

A. The Federal Circuit's Decision Conflicts With the Patent Act and This Court's Precedents

1. This Court's precedents are clear: For a patent claim to be anticipated and therefore invalid, the claimed invention itself must be found in the prior art, with "all the elements in combination which compose" the claimed invention. *Planing-Mach. Co.* v. *Keith*, 101 U.S. 479, 489 (1880). Near-identicality is not enough. Even where the invention combines various elements, some of them old, adding "[o]ne new and operative agency in the production of the desired result would give novelty to the entire combination." *Le Roy* v. *Tatham*, 63 U.S. 132, 139 (1860).

Even after the doctrine of anticipation/novelty was codified in §102 of the 1952 Patent Act, this Court confirmed the requirements of that section "have always existed in the statutory scheme" and are distinct from the non-obviousness requirement under §103. *Graham* v. *John Deere Co. of Kansas City*, 383 U.S. 1, 12 (1966). As Judge Learned Hand stated:

> No doctrine of the patent law is better established than that a prior patent or other publication to be an anticipation must bear within its four corners adequate directions for the practice of the patent invalidated.

Dewey & Almy Chem. Co. v. *Mimex Co.*, 124 F.2d 986, 989 (2d Cir. 1942).

Here, there is no dispute that the '755 Patent provided a new element not found in the prior art. The prior art proposed treating disease with human interferon-β, which could not be harvested in sufficient amounts. App., *infra*, 73a-74a. The '755 Patent overcame that barrier, describing and enabling a method to treat disease using an analogue, recombinant interferon-β made by non-human cells. But the Federal Circuit wrongly denied patent protection to that important and medically significant innovation.

2. To justify that result, the Federal Circuit invoked product-by-process case law, under which "an old product is not patentable even if it is made by a new process." *Amgen*, 580 F.3d at 1366. But that doctrine—as the name *product*-by-process implies—is about *products*, not methods of using products (such as methods of treatment). This Court has been clear that "a patentee who does not distinguish his product from what is old except by reference, express or constructive, to the process by which he produced it, cannot secure a monopoly on the product by whatever means produced." *Gen. Elec. Co.* v. *Wabash Appliance Corp.*, 304 U.S. 364, 373 (1938); accord *Cochrane* v. *Badische Anilin & Soda Fabrik*, 111 U.S. 293, 311 (1884) ("While a new process for producing [an old product] was patentable, the product itself could not be patented, even though it was a product made artificially for the first time.").

Just as "a new product may be patented" in product-by-process law "by reciting *source or process* limitations so long as the product is new and unobvious," *Amgen*, 580 F.3d at 1366 (emphasis added), source limitations can confer patentability on a new, unobvious method of treatment. The '755 Patent does not claim recombinant interferon-β itself; it claims methods of treatment with *recombinant* interferon-β made in a *non-human host cell—i.e.*, treatment with a product defined by source and process limitations. That method of treatment itself is new—it had never been performed in the prior art—and the jury found (and respondents did not appeal the jury's finding) that the method is not obvious.

The entire point of the '755 Patent, from its very first columns describing the problem to be solved, is Dr. Fiers's proof that recombinant interferon-β, even though structurally different from native interferon-β, has the same biological activity and can be used as a therapeutic in the same way that the native, human protein had been used. C.A. App. 136a-140a (37:18-46:37). The Federal Circuit found anticipation by expressly ignoring the '755 Patent's requirements that the interferon-β be recombinant and that it be produced in a non-human host cell. Yet these requirements made Dr. Fiers's claimed treatment method different from all prior art methods, an undeniable fact admitted by respondents. App., *infra*, 63a.

The Federal Circuit's denial of patentability ignores Congress's and this Court's clear instruction that novel methods of treatment are different from patenting a product. The Patent Act begins by separating claims to processes from claims to things (compositions of matter): "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter

* * * may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. §101. That distinction matters: An inventor may obtain a patent on the medical use of a natural product, like lithium to treat neurodegenerative disorders or human Factor VIII to treat hemophilia, even though the products themselves are "products of nature" and thus not eligible for patenting under 35 U.S.C. §101. Likewise, an inventor may obtain a patent on a new medical use for a decades-old product, even though the product itself is long past the era of patent protection. See, *e.g.*, *Perricone* v. *Medicis Pharm. Corp.*, 432 F.3d 1368, 1378 (Fed. Cir. 2005).

This Court recognized the fundamental distinction between method claims and product claims in *Association for Molecular Pathology* v. *Myriad Genetics, Inc.*, 569 U.S. 576 (2013), which concerned whether naturally occurring human DNA that has been isolated could be patented. The Court invalidated claims directed to human DNA sequences, but drew a critical distinction between product claims and method claims involving DNA: "It is important to note what is *not* implicated by this decision. First, there are no method claims before this Court. Had Myriad created an innovative method of manipulating genes while searching for the BRCA1 and BRCA2 genes, it could possibly have sought a method patent." *Id.* at 595. The Federal Circuit's decision defies *Myriad*'s clear directive that, even if a *product* is not patentable, that does not mean *methods* of using the product cannot be patented.

To be sure, a method of treatment using a recombinant protein could be rendered *obvious* by prior-art uses of a native, human protein. But here the jury found that Dr. Fiers's claimed treatment method was *not* obvi-

ous. This is not surprising given that Dr. Fiers invented his method in 1980, at the dawn of the biotechnology revolution. The Federal Circuit's holding, however, was not that Dr. Fiers's invention was obvious—respondents did not even appeal the jury's finding of non-obviousness. Instead, the Federal Circuit ruled that what Dr. Fiers did had been done before, a conclusion it reached by holding that the novel features of his invention are legally irrelevant. This was error.

The Federal Circuit's application of product-by-process law to method claims is wrong. That body of law makes eminent good sense where the patent claim is directed to a product that is a tangible thing. As this Court has made clear, one cannot obtain a patent on an old product merely by virtue of having invented a new way to make it. *Gen. Elec. Co.*, 304 U.S. at 373. That is because the tangible thing is the same, whether made by a new or old process. But methods are inherently different: by definition, a method patent is directed to *activities*, not physical things. Here, the claimed method can only be practiced by the use of a recombinant protein. That means that someone, at some time, must have performed the genetic engineering necessary to create the recombinant material, activities entirely absent from the prior art. Tellingly, when the Federal Circuit held that it would "defy all reason" and produce "absurd result[s]" to treat method claims as different, it cited no precedent in support of this newfound rule. App., *infra*, 14a-15a.

3. Having established that new, incorrect rule of law that requires courts to ignore new processes even in method-of-treatment claims, the Federal Circuit then compounded its error. It held that recombinant interferon-β made in a non-human cell and native, human

interferon-β are identical even though every witness agreed that they are different. This, too, ran afoul of *Myriad*, in which this Court distinguished between naturally occurring DNA and its man-made counterpart, complementary DNA (cDNA). See *Myriad*, 569 U.S. at 595. Even though it was conceded that the nucleotide sequence of cDNA is dictated by nature, "the lab technician unquestionably *creates something new when cDNA is made*" and thus cDNA "is distinct from the DNA from which it was derived." *Ibid.* (emphasis added).

The finding of the district court, based on the undisputed evidence at trial, was that recombinant interferon-β and native, human interferon-β differ in ways analogous to those at issue in *Myriad*. Native, human interferon-β is a 166-amino-acid protein with an attachment of sugars dictated by its production in human cells. App., *infra*, 8a-9a; C.A. App. 77878 (29:2-13). That is the protein that was used in the prior art references on which respondents relied for anticipation. Recombinant interferon-β has the same amino-acid sequence, but when Dr. Fiers created it in E. coli, he "unquestionably create[d] something new" because the glycosylation pattern—that is, the molecular structure of the polypeptide of the treatment method—is different from that in native, human interferon-β (or entirely absent where the recombinant molecule is made in E. coli). App., *infra*, 8a-9a; *id.* at 65a-77a; C.A. App. 24315. Indeed, Dr. Fiers's patent application begins by noting that there had been prior-art therapeutic uses of native, human interferon-β, but explains that his invention was to create a slightly different version of that protein, recombinantly, that could be used as a therapeutic. C.A. App. 118-121 (2:53-7:36). There was no evidence before the jury, and there is no

evidence at all, that any prior-art use of interferon-β employed the recombinant analogue.

In ruling that Dr. Fiers's invention was not novel and hence not patentable, the Federal Circuit went in a startling new direction. It allowed a jury to find anticipation where the claimed method of treatment undisputedly did not exist in the prior art. It essentially holds that all of Dr. Fiers's time and energy was wasted, because the express claim language requiring that the protein to be used for treatment be "recombinant" and made in a "non-human" host must be disregarded. The decision threatens an inventor's ability to patent a new method of treatment using a recombinant protein engineered to provide therapeutically effective activity in place of the scarce or unavailable human version.

B. The Federal Circuit's Decision Will Undermine Longstanding Incentives and Discourage Investment Essential to Developing New Therapeutic Treatments

The harm of that decision is difficult to overstate. Recombinant technology has enormous medical significance: The global recombinant-therapy market is estimated to be some $90 billion now, and growing annually. *Global Therapeutic Proteins Market Report 2020: Market was Valued at $93.14 Billion in 2018 and is Expected to Grow to $172.87 Billion through 2022*, Business Wire (Dec. 21, 2019), https://www.businesswire.com/news/home/20191223005228/en/Global-Therapeutic-Proteins-Market-Report-2020-Market-was-Valued-at-93.14-Billion-in-2018-and-is-Expected-to-Grow-to-172.87-Billion-through-2022---ResearchAndMarkets.com. The FDA has approved more than 140 recombinant proteins for therapeutic use following extensive and costly clinical development by their sponsors. *Recombinant Therapeutic Antibodies and*

Proteins Market, PharmiWeb (Dec. 17, 2020), https://www.pharmiweb.com/press-release/2020-12-17/recombinant-therapeutic-antibodies-and-proteins-market-share-and-trend-analysis-by-top-leading-playe. Half of the top ten therapeutic products by sales value are recombinant proteins.[4] These and other recombinant therapeutics help millions of people get the treatment that they need. Many diseases and conditions are caused by the human body failing to make, or failing to make enough of, a given human protein. Scientists and pharmaceutical inventors use recombinant techniques to replace or supplement proteins that the human body fails to make, allowing treatment of some of the most dire diseases and conditions. Hundreds of thousands of hemophilia patients inject themselves with recombinant Factor VIII, a synthetic analogue to a human protein that they do not make themselves. *Treatment of Hemophilia*, Centers for Disease Control and Prevention (July 17, 2020), https://www.cdc.gov/ncbddd/hemophilia/treatment.html. Recombinant Human Growth Hormone has largely replaced HGH harvested from cadavers. Marzieh Rezaei & Sayyed H. Zarkesh-Esfahani, *Optimization of production of recombinant human growth hormone in* Escherichia coli, 17(7) J. Rsch. Med. Sci. 681 (2012). Recombinant human insulin replaced porcine-and bovine-sourced insulin and made it possible for millions of diabetes sufferers to manage the disease and lead normal lives. Wolfgang Landgraf & Juergen Sandow, *Recombinant Human Insulins—Clinical Efficacy and Safety in*

---

[4] Humira® (adalimumab); Keytruda® (pembrolizumab); Stelara® (ustekinumab); Eylea® (aflibercept); and Opdivo® (nivolumab). Derek Burkhard, et al., *The Top 10 Best-Selling Drugs of 2020*, Scrip (Apr. 23, 2021), https://scrip.pharmaintelligence.informa.com/SC144160/The-Top-10-Best-Selling-Drugs-Of-2020.

Diabetes Therapy, 12(1) Eur. Endocinology 12 (2016).[5] Recombinant granulocyte colony-stimulating factor has transformed cancer treatment by protecting chemotherapy patients (in the United States approximately 650,000 people per year receive chemotherapy) from life-threatening infections due to their compromised immune systems. J. Rusthoven, et al., *Use of granulocyte colony-stimulating factor (G-CSF) in patients receiving myelosuppressive chemotherapy for the treatment of cancer. Provincial Systemic Treatment Disease Site Group*, 2(4) Cancer Prev. Control 179 (1998); *Preventing Infections in Cancer Patients*, Centers for Disease Control and Prevention (Nov. 10, 2020), https://www.cdc.gov/cancer/preventinfections/providers.htm#:~:text=Each%20year%2C%20about%20650%2C000%20cancer,clinic%20in%20the%20United%20States. Recombinant erythropoietin has counteracted some of the worst side effects suffered by dialysis patients (of which there are nearly 500,000 in the United States alone) due to the inability of their blood to carry sufficient oxygen. J. Cody, et al., *Recombinant human erythropoietin for chronic renal failure anaemia in pre-dialysis patients*, Cochrane Database Syst. Rev. (2005); *Kidney Disease Statistics for the United States*, National Institute of Health (2015), https://www.niddk.nih.gov/health-information/health-statistics/kidney-disease#:~:text=More%20than%20661%2C000%20Americans%20have,with%20a%20functioning%20kidney%20transplant. Humira® (recombinant adalimumab) is approved to treat moderate to severe rheumatoid arthritis (approximately 1.5 million Americans

---

[5] As of 2015, insulin was used by approximately six million Americans. *Fast Facts Data and Statistics About Diabetes*, American Diabetes Association (Dec. 2015), https://professional.diabetes.org/sites/professional.diabetes.org/files/media/fast_facts_12-2015a.pdf.

had rheumatoid arthritis as of 2007), plaque psoriasis (125 million people worldwide suffer from psoriasis), moderate to severe Crohn's disease (approximately 593,000 to 780,000 people in the United States have been diagnosed with Crohn's disease), ulcerative colitis (approximately one million people in the United States have ulcerative colitis), among other indications. *Humira*, https://www.humira.com/; *Arthritis by the Numbers* at 31, Arthritis Foundation (2019), https://www.arthritis.org/getmedia/e1256607-fa87-4593-aa8a-8db4f291072a/2019-abtn-final-march-2019.pdf; *Psoriasis Statistics*, National Psoriasis Foundation (Oct. 8, 2020), https://www.psoriasis.org/psoriasis-statistics/; Michael L. Ganz, et al., *The Economic and Health-related Impact of Crohn's Disease in the United States: Evidence from a Nationally Representative Survey*, 22(5) Inflamm. Bowel Dis. 1032 (2016); Bruce Goldman, *Stanford scientists link ulcerative colitis to missing gut microbes*, Stanford Medicine (Feb. 25, 2020), https://med.stanford.edu/news/all-news/2020/02/stanford-scientists-link-ulcerative-colitis-to-missing-gut-micro.html#:~:text=About%201%20million%20people%20in,condition%20to%20a%20missing%20microbe. Monoclonal antibodies derived from human Covid-19 survivors and produced recombinantly are used (in combination with a murine-derived antibody) to treat the most seriously affected patients. *Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibodies for Treatment of COVID-19*, U.S. Food & Drug Administration (Feb. 9, 2021), https://www.fda.gov/ news-events/press-announcements/coronavirus-covid-19update-fda-authorizes-monoclonal-antibodies-treatment-covid-19-0. In each of these instances, investment in the development of an effective recombinant protein revolutionized the treatment of a disease.

Literally hundreds of other recombinant proteins are believed to be in pre-clinical or clinical development for treating diseases. But such development requires immense resources: The most recent studies show that bringing a new biologic medicine (the category in which recombinant proteins fall) to market costs on average $2.6 billion. Joseph A. DiMasi, et al., *Innovation in the pharmaceutical industry: New estimates of R&D costs*, 47 J. of Health Econ. 20 (2016). And this work is risky: for every such medicine that comes to market, dozens of others fail. See, *e.g.*, Biotechnology Innovation Organization, *Clinical Development Success Rates 2006-2015*, at 3 (2016).[6] Patent protection provides a vital incentive that makes it possible to create these groundbreaking medical innovations. By providing time-limited exclusivity, patents allow research-based companies to use the revenue from the handful of their successes to pay for creating the next generation of new treatments.

The Federal Circuit's decision stands to upend this careful balance. Holding that a method of treatment with newly created recombinant material is anticipated by a prior-art method of treatment with non-recombinant material upsets the settled expectations of all those currently working on new recombinant medicines. Those settled expectations matter because, as noted above, the development of new medical treatments using recombinant technology is enormously expensive. For companies to continue to invest in such high-risk research and development, robust and predictable patent protection is essential.

---

[6] https://www.bio.org/sites/default/files/legacy/bioorg/docs/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf.

By holding that a method of treatment with a recombinant protein is anticipated by treatment with the non-identical native, human protein of which it is an analogue, the Federal Circuit's decision dramatically changes the incentives and threatens to curtail development in these desperately needed areas.

C. This Is an Appropriate Vehicle To Address These Important Issues

This case presents a clean, undisputed set of facts. Recombinant interferon-β and native, human interferon-β contain the same sequence of 166 amino acids dictated by nature, but due to the different sugar groups attached to the amino acids the two molecules—and indeed, the amino acids themselves—are not the same. There is no dispute that no prior art reference disclosed each of the elements of the '755 Patent's claims. The Federal Circuit's decision thus presents a pure question of law, which this Court would review de novo.

From those undisputed facts, the Court's clarification (and, Biogen submits, re-confirmation) of the law of anticipation would have widespread impact across a range of cases and technologies, incentivizing medical innovation and providing needed guidance to biopharmaceutical companies as they evaluate which needed therapies they can (or cannot) economically pursue.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted,

NICHOLAS GROOMBRIDGE
ERIC ALAN STONE
PETER SANDEL
JENNY C. WU
JOSEPHINE YOUNG
PAUL, WEISS, RIFKIND
WHARTON & GARRISON
LLP
1285 Ave. of the Americas
New York, NY 10019
(212) 373-3000

JEFFREY A. LAMKEN
Counsel of Record
MOLOLAMKEN LLP
The Watergate, Suite 500
600 New Hampshire Ave., N.W.
Washington, D.C. 20037
(202) 556-2000
jlamken@mololamken.com

Counsel for Petitioner

MAY 2021

APPENDIX

APPENDIX A

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

[AS AMENDED]

No. 2019-1133

BIOGEN MA INC.,

Plaintiff-Appellee,

v.

EMD SERONO, INC.,
PFIZER INC.,

Defendants-Appellants,

BAYER HEALTHCARE PHARMACEUTICALS INC.,
NOVARTIS PHARMACEUTICALS CORPORATION

Defendants.

Appeal from the United States District Court for the District of New Jersey in No. 2:10-cv-02734-CCC-MF, United States District Judge Claire C. Cecchi.

OPINION

September 28, 2020

NICHOLAS P. GROOMBRIDGE, Paul, Weiss, Rifkind, Wharton & Garrison LLP, New York, NY, argued for plaintiff-appellee. Also represented by PETER SANDEL, ERIC ALAN STONE, JENNY CHIA CHENG WU, JOSEPHINE

YOUNG; DAVID J. BALL, JR., Washington, DC; JOHN D. TORTORELLA, KEVIN H. MARINO, Marino Tortorella & Boyle, PC, Chatham, NJ.

MARK ANDREW PERRY, Gibson, Dunn & Crutcher LLP, Washington, DC, argued for defendants-appellants. Also represented by CHRISTINE RANNEY, Denver, CO; WAYNE M. BARSKY, TIMOTHY P. BEST, Los Angeles, CA; JAYSEN CHUNG, San Francisco, CA.

BRUCE GENDERSON, Williams & Connolly LLP, Washington, DC, for amicus curiae Bayer Healthcare Pharmaceuticals Inc. Also represented by DAVID I. BERL, SETH BOWERS, DAVID M. KRINSKY.

Before NEWMAN, LINN, and HUGHES, *Circuit Judges*.

LINN, *Circuit Judge*.

This appeal arises from a suit filed by Biogen MA, Inc. ("Biogen") against EMD Serono, Inc. and Pfizer, Inc. (collectively "Serono") in the District of New Jersey.[1] The suit alleged contributory and induced infringement of Biogen's U.S. Patent Number 7,588,755 ("'755 patent") by the sale and marketing in the United States of Rebif, a recombinant interferon-β ("IFN-β") product used for the treatment of Multiple Sclerosis ("MS"). After a five-week trial, a jury found that the '755 patent claims were anticipated by two references teaching the use of native IFN-β to treat viral diseases: Kingham *et al.*, *Treatment of HBsAg-positive Chronic Active Hepatitis with Hu-*

[1] Biogen also asserted infringement claims against Bayer Healthcare Pharmaceuticals Inc. ("Bayer") and Novartis Pharmaceuticals Corp. ("Novartis"). The actions against Bayer and Novartis were severed from those giving rise to this appeal. Order Granting Bayer's Motion to Sever, Oct. 27, 2017, ECF No. 743. Bayer filed an amicus brief here.

man Fibroblast Interferon, 19(2) Gut 91 (1978) ("Kingham") and Sundmacher *et al.*, *Human Leukocyte and Fibroblast Interferon in a Combination Therapy of Dendritic Keratitis*, 208(4) Albrecht von Graefes Archiv für Klinische & Experimentelle Opthalmologie 229 (1978) ("Sundmacher"). The jury also held the asserted claims not invalid for lack of enablement or written description, or for obviousness. Finally, the jury held that patients and prescribers directly infringed the asserted claims and that Serono contributorily infringed the claims but did not induce infringement thereof.

On cross-motions, the district court granted judgment as a matter of law ("JMOL") of no anticipation in favor of Biogen and conditionally granted a new trial on anticipation. *In re Biogen '755 Patent Litig.*, 335 F. Supp. 3d 688 (D.N.J. 2018) ("*Biogen I*"). The district court also ruled in favor of Biogen: sustaining the jury's verdict of no invalidity based on written description or enablement; overturning the verdict of no induced infringement; sustaining the verdict of contributory infringement; and holding that the '755 patent claims were not patent ineligible. *Id.* Serono appeals the district court's JMOL rulings on anticipation, written description, enablement, contributory infringement, induced infringement and patent eligibility. We have jurisdiction under 28 U.S.C. § 1295(a).

Because a reasonable jury could find the claims of the '755 patent anticipated on the record presented in this case, we reverse the district court's JMOL of no anticipation and its conditional grant of new trial on that ground. We remand with instructions to reinstate the jury verdict of anticipation. We need not and do not address the other grounds asserted on appeal.

I

The '755 patent is directed to a method of treating a viral condition, a viral disease, cancers or tumors, by administration of a pharmaceutically effective amount of a recombinant polypeptide related to human interferon-β ("IFN-β"). The human immune system naturally produces IFN-β in small amounts, and it is undisputed that IFN-β harvested from human cells ("native IFN-β") was used in the prior art to treat viral conditions. See '755 patent, col. 2, l. 53-col. 4, l. 22.

Representative claim 1 of the '755 patent reads:

> 1. A method for immunomodulation or treating a viral condition[ ], a viral disease, cancers or tumors comprising the step of administering to a patient in need of such treatment a therapeutically effective amount of a composition comprising:
>
> a recombinant polypeptide produced by a non-human host transformed by a recombinant DNA molecule comprising a DNA sequence selected from the group consisting of:
>
> (a) DNA sequences which are capable of hybridizing to any of the DNA inserts of G-pBR322(Pst)/HFIF1, G-pBR322(Pst)/HFIF3 (DSM 1791), G-pBR322(Pst)/HFIF6 (DSM 1792), and GpBR322(Pst)/HFIF7 (DSM 1793) under hybridizing conditions of 0.75 M NaCl at 68° C. and washing conditions of 0.3 M NaCl at 68° C., and which code for a polypeptide displaying antiviral activity, and
>
> (b) DNA sequences which are degenerate as a result of the genetic code to the DNA sequences defined in (a);

> said DNA sequence being operatively linked to an expression control sequence in the recombinant DNA molecule.

'755 patent, col. 49, l. 59-col. 50, l. 12. Dependent claim 2 replaces the "capable of hybridizing" limitation with a selection from two particular DNA sequences, one of which is the DNA sequence of human interferon-beta. *Id.* at col. 50, ll. 13-52. Claims 1 and 2 thus define the claimed polypeptide by reference to the DNA sequence inserted into the host during the recombinant manufacture of the polypeptide. Claim 3, dependent from claim 1, limits the polypeptide to a particular linear polypeptide sequence. Because the claimed IFN-β DNA and polypeptide sequences are derived from human IFN-β, it is indisputable that native human IFN-β is capable of hybridizing with the DNA sequences in claim 1, is produced by one of the DNA sequences laid out in claim 2, and comprises the amino acid sequence set out in claim 3. See J.A. 47784 (Fiers Aff. To the Canadian Patent Office, indicating that the recombinant IFN-β was derived from human IFN-β cDNA); J.A. 77897 (Dr. Green Test., testifying that the sequences claimed in claim 1 are "DNA that will hybridize to one of the four human beta interferon clones"); J.A. 77904 (Dr. Green Test., testifying that accused-product Rebif is capable of hybridizing to one or more of the DNA inserts because the DNA sequence it used is identical to the published sequence of human IFN-β). For purposes of this opinion, we refer to "recombinant IFN-β" as shorthand for the recombinant protein that meets these claim limitations.

During *Markman*, the district court held that claim 1 covers a "one-step method of 'administering' to a patient in need the specified recombinant HuIFN-β." Markman Opinion at 17, Mar. 28, 2016, ECF No. 403. The district

court considered the claimed "produced" and "transformed" steps "merely descriptive of the recombinant polypeptide to be administered," i.e. merely source limitations. *Id.* at 15. The district court also held that it was "unclear that [the] method of treatment claim can be treated as a product-by-process claim," and that it was "aware of no binding precedent requiring method of treatment claims to be treated as product-by-process claims in the claim construction context." *Id.* at 14. The district court did not construe "polypeptide," "therapeutically effective amount," or "antiviral activity," and neither party asked the court to consider whether the claims covered the linear sequence of amino acids or the three-dimensional structure of the protein.

Biogen, Serono, and Bayer all moved for summary judgment. Before Bayer was severed, Bayer argued that it was entitled to summary judgment of anticipation because the claimed recombinant IFN-β and the prior art native IFN-β shared the same linear amino acid sequence. The district court denied Bayer's motion, holding, *inter alia*, that the claims require the polypeptide to have "antiviral activity" and be administered in a "therapeutically effective amount." Summary Judgment Opinion at 28, Jan. 9, 2018, ECF No. 892. The district court concluded that those requirements necessitate that the polypeptide "be folded into its appropriate three-dimensional structure," and that Bayer was therefore not entitled to summary judgment of anticipation by merely showing that the amino acid sequence of recombinant IFN-β and the amino acid sequence of native IFN-β were identical. *Id.*

After a five-week trial, Biogen and Serono both moved for JMOL under Federal Rule of Civil Procedure 50(a). The district court deferred ruling until the jury verdict.

Among other issues, the court submitted anticipation, obviousness, enablement, written description, and contributory and induced infringement to the jury. In its charge on anticipation, the district court told the jury that "[t]he term 'polypeptide' means 'a linear array of amino acids connected one to the other by peptide bonds between the αamino and carboxy groups of adjacent amino acids,'" and that the jury "must accept my definition of these words in the claims as correct." Final Jury Instructions at 17, Feb. 21, 2018, ECF No. 968. Biogen did not object to these instructions and did not request any instruction defining the polypeptide in terms of its three-dimensional structure or requiring identity of the three-dimensional structures of native IFN-β and recombinant IFN-β proteins to establish anticipation.

The jury held, *inter alia*, that all claims in the '755 patent were invalid as anticipated by native IFN-β; not invalid for obviousness, lack of enablement or lack of written description; and that Serono was liable for contributory infringement but not induced infringement. Jury Verdict Form at 1-6, Feb. 23, 2018, ECF No. 977.

Both parties renewed their JMOL motions. As relevant here, the district court granted Biogen's motion of no anticipation as a matter of law. *Biogen I*, 335 F. Supp. 3d at 713. In a comprehensive opinion, the district court held that no reasonable jury could find anticipation under Serono's reading of the claims. First, applying a structural reading of the recombinant limitations, the district court held that Serono had not identified any prior art that disclosed "treatment with a 'therapeutically effective amount' of a composition comprising a 'recombinant' interferon-β polypeptide produced in a 'non-human host' that had been 'transformed by a recombinant DNA molecule.'" *Id.* at 704. **[JA21]**. The district court reasoned

that because treatment in the prior art entailed administration of native IFN-β, which was undisputedly not recombinantly produced, no reasonable jury could find anticipation. *Id.* at 705. The district court cited but did not distinguish *Amgen Inc.* v. *Hoffman-La Roche Ltd.*, 580 F.3d 1340 (Fed. Cir. 2009), which analyzed anticipation of a claimed recombinant erythropoietin ("EPO") by prior art urinary (i.e. natural) EPO. *Biogen I*, 335 F. Supp. 3d at 1367. The district court declined to apply a product-by-process analysis to a product-by-process limitation contained within a method of treatment claim, concluding that no precedent required such an analysis and that the policy informing product-by-process claims—to enable an inventor to claim an otherwise difficult-to-define product—was inapplicable to the instant method of treatment claims. *Id.* at 712-13.

In the alternative, the district court held that no reasonable jury could have found anticipation even applying a product-by-process analysis. *Id.* at 705-11. The district court explained that because the claims required administration of a "therapeutically effective amount" of a recombinant polypeptide that "displays antiviral activity," the product resulting from the claimed recombinant process is defined by the folded three-dimensional structure of the protein. *Id.* at 705 (discussing Summary Judgment Opinion at 28, Jan. 9, 2018, ECF No. 892). The district court held that the jury lacked substantial evidence that the native IFN-β protein as disclosed in Kingham and Sundmacher was structurally or functionally identical to the claimed three-dimensional recombinant IFN-β protein. *Id.*

With respect to structural identity, the district court explained that the glycosylation patterns in native IFN-β and recombinant IFN-β were different, and that this

change affected the three-dimensional structure of the protein. *Id.* The district court—relying on expert testimony by Serono's expert, Dr. Lodish, and statements found in a post-priority date reference created by InterPharm Laboratories Ltd. entitled "Comparative Biochemical Analysis of Native Human Fibroblast lnterferon and Recombinant Beta Interferon Expressed by Chinese Hamster Ovary Cells" ("InterPharm")—concluded that native and recombinant IFN-β were not *identical* but merely very similar. *Id.* at 706-07. The district court opined that the structural differences alone preclude anticipation. *Id.* at 710-11 (relying primarily on this court's decision in *Amgen*, 580 F.3d at 1367-69, in which we affirmed a holding of no anticipation based on structural differences). Finally, the district court discounted the conclusion in the InterPharm study that recombinant IFN-β and native IFN-β were identical. It held that there was no substantial evidence that the generic "native IFN-β" analyzed in the InterPharm study and found to be identical to recombinant IFN-β was the same native IFN-β taught in the prior art. *Id.* at 708.

As for functional identity, the district court held that the relative ease of manufacture of recombinant IFN-β in large quantities functionally distinguished it from native IFN-β. *Id.* at 709-10.

For these reasons, the district court granted JMOL of no anticipation. *Id.* at 713. The district court also conditionally granted Biogen's motion for a new trial on anticipation "[f]or the same reasons the Court grants Biogen's JMOL motion." *Id.* The district court added that the trial was complex and was "noticeably focused on issues other than anticipation," such that that the jury verdict deserved close scrutiny. *Id.*

Serono appeals. We have jurisdiction under 28 U.S.C. § 1295.

II

We review the grant of JMOL and the grant of new trial under the law of the regional circuit. *Uniloc USA, Inc.* v. *Microsoft Corp.*, 632 F.3d 1292, 1301, 1309 (Fed. Cir. 2011). The Third Circuit reviews the grant of JMOL for a fact question de novo, affirming "only if, viewing the evidence in the light most favorable to the nonmovant and giving it the advantage of every fair and reasonable inference, there is insufficient evidence from which a jury reasonably could find liability." *Lightning Lube, Inc.* v. *Witco Corp.*, 4 F.3d 1153, 1166-67 (3d Cir. 1993); *Garzier ex rel. White* v. *City of Phila.*, 328 F.3d 120, 123 (3d Cir. 2003) ("A district court should grant such a motion only if, viewing all the evidence in favor of the nonmoving party, no reasonable jury could find liability on a particular point."). The Third Circuit reviews the conditional grant of a new trial against the weight of the evidence for an abuse of discretion, "unless the court's denial is based on the application of a legal precept, in which case the standard of review is plenary." *Lightning Lube*, 4 F.3d at 1167.

III

A claim is anticipated only if "each and every [limitation] is found within a single prior art reference." *Summit 6, LLC* v. *Samsung Elecs. Co.*, 802 F.3d 1283, 1294 (Fed. Cir. 2015). Anticipation is a factual question and thus within the ordinary provenance of the jury. *Lighting Ballast Control LLC* v. *Phillips Elecs. N. Am. Corp.*, 790 F.3d 1329, 1340 (Fed. Cir. 2015).

In evaluating the evidentiary record presented to the jury on the question of anticipation, the district court: (1) declined to apply a product-by-process analysis to the

claimed recombinant IFN-β source limitation; and (2) in its alternative ground analysis, required identity of three-dimensional structures not specifically recited in the claims rather than the claimed and lexicographically defined "polypeptide." Both of these determinations led to an erroneous conclusion on anticipation.

A. The Recombinant Source of the Polypeptide

The district court, focusing on the process of making recombinant IFN-β, concluded that it need not analyze whether native IFN-β and recombinantly produced IFN-β were identical because neither Kingham nor Sundmacher prior art reference taught a method of treatment *using recombinant IFN-β*. *Biogen I*, 335 F. Supp. 3d at 704. It categorized the "produced" and "transformed" limitations as meaningful "source limitations." *Id.* at 711-12. The district court was convinced that because the recombinant source limitations here overcame the shortcoming of the prior art—namely, the unavailability of native IFN-β in sufficient quantity to facilitate practical treatment—the recombinant nature of the claimed IFN-β "lies at the heart of the benefit of this invention" [and] should be given "force and effect in the anticipation analysis.'" *Id.* (quoting Biogen's statements at JMOL hearing, Trial Tr. 6/6/18 at 12:7-10). The district court reasoned that no binding precedent required it to apply a product-by-process analysis to a limitation contained in a method of treatment claim, and held that the rationale underlying the use of product-by-process claims—to allow claiming of an otherwise difficult-to-define invention, see *SmithKline*, 439 F.3d at 1315—did not apply to the claims here because the "product" itself was sufficiently described. *Biogen I*, 335 F. Supp. 3d. at 713. The district court thus concluded there could be no anticipation, re-

gardless of whether Serono had shown the identity of native IFN-β and recombinant INF-β.

Serono contends that Biogen has waived any argument that the recombinant source of the IFN-β can alone confer novelty because Biogen's pre-verdict JMOL motion only argued that native IFN-β and recombinant IFN-β were not identical. We find no waiver. The source limitation was one of the bases for Biogen's argument of non-identity and was considered by the district court at Summary Judgment and in its opinion on JMOL.

On the merits, Serono asserts that a source limitation alone cannot confer novelty unless the product itself is novel. Serono argues that the district court erred by holding that the lack of a recombinantly produced IFN-β product in the prior art compelled a finding of no anticipation. Biogen argues that the source of the IFN-β matters is an independent limitation.

We agree with Serono. The district court's refusal to consider the identity of recombinant and native IFN-β runs afoul of the longstanding rule that "an old product is not patentable even if it is made by a new process." *Amgen*, 580 F.3d at 1366. See also *Gen. Elec. Co.* v. *Wabash Appliance Corp.*, 304 U.S. 364, 373 (1938) ("[A] patentee who does not distinguish his product from what is old except by reference, express or constructive, to the process by which he produced it, cannot secure a monopoly on the product by whatever means produced."); *Cochrane* v. *Badische Anilin & Soda Fabrik*, 111 U.S. 293, 311 (1884) ("While a new process for producing [an old product] was patentable, the product itself could not be patented, even though it was a product made artificially for the first time."); *SmithKline Beecham Corp.* v. *Apotex Corp.*, 439 F.3d 1312, 1317 (Fed. Cir. 2006) ("It has long been established that one cannot avoid anticipa-

tion by an earlier product disclosure by claiming the same product . . . as produced by a particular process.").

In *Amgen*, we explained that a claim to a recombinant EPO composition must be analyzed for novelty by comparing the recombinant EPO to the prior art urinary EPO. We further explained that simply because prior art urinary EPO was not made recombinantly was not enough to avoid anticipation as a matter of law.[2] 580 F.3d at 1370 ("To prove invalidity, Roche had to show that recombinant EPO was the same as urinary EPO, *even though urinary EPO was not made recombinantly*.") (emphasis added). The key question was "whether the production of EPO by recombinant technology resulted in a new product," *id.* at 1367, or, "[i]n other words, does the source limitation 'purified from mammalian cells grown in culture' distinguish recombinant EPO from [prior art] urinary EPO?" *Id.*

The nature of the origin or source of the composition recited in the claims at issue in this case is, in all relevant respects, identical to that considered in *Amgen*. As in *Amgen*, the recombinant origin of the recited composition cannot alone confer novelty on that composition if the product itself is identical to the prior art non-

---

[2] The key claim in *Amgen* read: "A pharmaceutical composition comprising a therapeutically effective amount of human erythropoietin and a pharmaceutically acceptable diluent, adjuvant or carrier, wherein said erythropoietin is purified from mammalian cells grown in culture." 580 F.3d at 1364. An additional independent claim in a related patent read: "A non-naturally occurring glycoprotein product of the expression in a mammalian host cell of an exogenous DNA sequence comprising a DNA sequence encoding human erythropoietin said product possessing the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells." *Id.* In relevant part, we applied the same analysis to both claims.

recombinant product. The requirements that the claimed polypeptide is "recombinant" and "produced by a non-human host transformed by a recombinant DNA molecule" (in the case of Claim 1 of the '755 patent) describe the process by which the product, i.e. the "polypeptide," is formed. These are not additional structural limitations. See *Purdue Pharma L.P.* v. *Epic Pharma, LLC*, 811 F.3d 1345, 1353 (Fed. Cir. 2016) (holding that because a source limitation of a composition "has no effect on its structure . . . [that] limitation . . . cannot be a structural limitation"). The key question for anticipation here, as in *Amgen*, is thus whether the recombinant *product* is identical to the prior art *product*—not whether the prior art product was made recombinantly.

Biogen argues that *Amgen* is limited to composition claims and is not applicable to the method of treatment claims at issue here. To support this proposition, Biogen relies on general statements in product-by-process cases such as *In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985) (applying product-by-process analysis for "an otherwise patentable *product*") (emphasis added), and the well-recognized distinction patent law draws between the scope of composition and method of treatment claims. See, *e.g.*, *Ass'n for Molecular Pathology* v. *Myriad Genetics, Inc.*, 569 U.S. 576, 595 (2013) (recognizing the distinct scope for composition and method of treatment claims in the context of 35 U.S.C. § 101).

Biogen's only basis for novelty of the method of treatment claims at issue here is the novelty of the recombinant IFN-β composition that is administered. That composition is claimed in terms of the process by which it is manufactured. If the novelty of the recombinant IFN-β *composition* requires comparing its structure to the structure of native IFN-β, as *Amgen* requires, it would

defy all reason to excuse that analysis for a method of administration claim using that composition. Such a rule could have the absurd result that a recombinant composition could be non-novel, the method of administration could be non-novel, but the method of administration of the composition defined by the process of its manufacture would be novel as a matter of law.

There is no logical reason why the nesting of a product-by-process limitation within a method of treatment claim should change how novelty of that limitation is evaluated. Indeed, we have previously applied product-by-process analysis to a nested limitation. In *Purdue Pharma*, we interpreted a claim to "an oral dosage form comprising . . . oxycodone hydrochloride active pharmaceutical ingredient having less than 25 ppm 14-hydroxy[ ], wherein at least a portion of the 14-hydroxy [ ] is derived from 8α[ ] during conversion of oxycodone free base to oxycodone hydrochloride" as including a product-by-process limitation; namely, the 14-hydroxy as derived. *Purdue Pharma*, 811 F.3d at 1353 (emphasis omitted). Similar to our analysis here, the court in *Purdue Pharma* held that it was appropriate to focus on the identity of the products of the claimed and prior art processes, and not on the source limitation, in analyzing obviousness. See *id.* at 1353-54. The nesting of the product-by-process limitation within a method of treatment claim does not change the proper construction of the product-by-process limitation itself.

We are also unpersuaded by the district court's and Biogen's reasoning that a product-by-process-type analysis is inappropriate here because the composition was otherwise capable of definition other than by the process. That argument is precluded by *Amgen*, where the product was also well-defined in the claims: "human erythro-

poietin . . . wherein said erythropoietin is purified from mammalian cells grown in culture." 580 F.3d at 1364. Furthermore, as noted *supra*, the rule in *Amgen* is a necessary outgrowth of the black-letter legal principle that an old product made by a new process is not novel and cannot be patented. Logic compels extending that rule to the present case; an old method of administration of an old product made by a new process is not novel and cannot be patented.

Biogen is certainly correct that the scope of composition and method of treatment claims is generally subject to distinctly different analyses. But where, as here, the novelty of the method of administration rests wholly on the novelty of the composition administered, which in turn rests on the novelty of the source limitation, the *Amgen* analysis will necessarily result in the same conclusion on anticipation for both forms of claims.

Finally, the district court erred in considering the advantages of the *recombinant process*—the new capability of manufacturing sufficient quantities of IFN-β through recombinant technology—as a reason not to apply a product-by-process analysis. See *Biogen I*, 335 F. Supp. 3d at 713. That consideration may well be relevant in considering the novelty of the recombinant *process*, but, a new process, regardless of its novelty, does not make an old product created by that process novel. This does not fail to give "force and effect" to the heart of the claimed invention; it protects the public from attempts to excise old products from the public domain.

Because a proper anticipation analysis of the claims in the '755 patent turns not on the source of the claimed polypeptide but on a comparison of the claimed recombinant polypeptide and the prior art native polypeptide, the district court erred in concluding that the mere absence

of recombinantly produced IFN-β in the prior art was sufficient to grant JMOL of no anticipation.

B. The Three-Dimensional Structure of the Polypeptide

The district court also held that even applying a product-by-process type analysis, no reasonable jury could have found anticipation because the jury lacked sufficient evidence of identity between the claimed recombinant "polypeptide" and the native IFN-β. In particular, the district court concluded that just because recombinant and native IFN-β "share the same linear amino acid sequence is not enough for purposes of anticipation." *Id.* at 705. The district court took the position that native polypeptide anticipates the "recombinant polypeptide" only if their respective folded three-dimensional proteins share identical structure and function. *Id.* The district court reasoned that without a disclosure in the prior art of such three-dimensional protein, a showing of the native polypeptide alone would not necessarily produce "antiviral activity" when administered in a "therapeutically effective amount" as recited in the claims. *Id.* (citing Summary Judgment Opinion at 28, ECF No. 892). This was error.

The "product" administered in the claimed method is the "polypeptide." See '755 patent, col. 49, ll. 59-64 ("A method . . . comprising the step of administering . . . a therapeutically effective amount of a composition comprising: a recombinant polypeptide produced by a non-human host . . . ."). As noted *supra*, the key question for anticipation is whether the native "polypeptide" is identical to the "polypeptide" "produced by" the recited recombinant process.

Biogen explicitly defined "polypeptide" in the '755 patent:

> Polypeptide—A linear array of amino acids connected one to the other by peptide bonds between the α-amino and carboxy groups of adjacent amino acids.

'755 patent, col. 8, ll. 62-64. The "polypeptide" structure is thus defined by reference to its "linear" array, without regard to its folded protein structure. The district court charged the jury with this definition, adding that the jury "must accept my definition of these words in the claims as correct." Final Jury Instructions at 17, ECF No. 968. Biogen did not object to this charge and did not ask the court for a jury instruction requiring identity of the folded protein structures.

As the district court recognized on summary judgment, "Biogen does not dispute that '[t]he sequential order of the amino acid residues for native IFN-β is the same as the sequential order of the amino acid residues for recombinant IFN-β.'" Summary Judgment Opinion at 27, ECF No. 892. See also Biogen Brief at 19. Thus, the native IFN-β polypeptide and the claimed recombinant IFN-β polypeptide are identical for purposes of the instant claim.

Biogen argues that the district court was correct in requiring identity not just of the polypeptide, but also of the folded proteins, because the claims require the administration of "*a therapeutically effective amount* of a composition" and that the DNA sequences in the claims must "code for a polypeptide displaying *antiviral activity*." Biogen asserts that only three-dimensional proteins can be therapeutically effective and have antiviral activity, and therefore that the "product" to be analyzed for novelty is the folded three-dimensional protein, not just the amino acid sequence.

Biogen is incorrect. First, Biogen's argument fails to give effect to Biogen's explicit definition of "polypeptide" in the specification. We must respect this lexicographic choice. See *Edward Lifesciences LLC* v. *Cook Inc.*, 582 F.3d 1322, 1329 (Fed. Cir. 2009) ("[W]e will adopt a definition that is different from the ordinary meaning when 'the patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in . . . the specification'" (quoting *CCS Fitness, Inc.* v. *Brunswick Corp.*, 288 F.3d 1359, 1366-67 (Fed. Cir. 2002))). Biogen does not attempt to square its theory with the definition in the specification.

Second, Biogen draws the wrong conclusion from the claimed antiviral activity limitation. The claims, in calling for antiviral activity, do not recite any specific folded three-dimensional structure that gives rise to that activity. While it is indisputable that an amino acid sequence alone cannot give rise to antiviral activity, it is also indisputable that every linear sequence of amino acids will fold into *some* three-dimensional configuration. The claimed antiviral activity can arise from the administration of any three-dimensional protein with a linear amino acid sequence identical to the claimed recombinant "polypeptide."

Finally, and importantly, Biogen did not ask for a jury instruction on anticipation that required comparing the three-dimensional protein structures of prior art IFN-β and the claimed recombinant IFN-β. Neither Biogen nor the district court can reframe the anticipation inquiry on JMOL to focus on the unclaimed three-dimensional protein structure, where the jury was instructed, without objection, to decide anticipation based on the linear amino acid sequence. See *Finjan, Inc.* v. *Blue Coat Sys., Inc.*, 879 F.3d 1299, 1306 (Fed. Cir. 2018) ("[I]t is too late

at the JMOL stage to . . . adopt a new and more detailed interpretation of the claim language and test the jury verdict by that new and more detailed interpretation." (quoting *Hewlett-Packard Co.* v. *Mustek Sys., Inc.*, 340 F.3d 1314, 1321 (Fed. Cir. 2003))).

The jury was correctly instructed that "to be entitled to a patent, the invention must actually be 'new.'" J.A. 81262. It is undisputed that the prior art here teaches the administration of native IFN-β that has a linear amino acid sequence identical to the linear amino acid sequence of the recited recombinant IFN-β and that shows antiviral activity. See '755 patent, col. 3, ll. 4-14. The jury thus had sufficient evidence to find that native IFN-β polypeptide is identical to recombinant IFN-β polypeptide, was administered in therapeutically effective amounts, and showed antiviral activity in the prior art. The district court thus erred in granting JMOL of no anticipation.[3]

IV. CONDITIONAL GRANT OF NEW TRIAL

The district court also conditionally granted a new trial on anticipation. The district court's grant of a new trial was based on the same legal errors supporting its grant of JMOL. *Biogen I*, 335 F. Supp. 3d at 713 ("For the same reasons the Court grants Biogen's JMOL motion, the Court conditionally orders a new trial on anticipation."). None of the additional considerations noted by the district court in support of its conditional grant of a new trial are independently sufficient to support its deci-

[3] Because the proper construction of the claims does not require comparison of the three-dimensional structure of prior art native IFN-β and recombinant IFN-β, we need not consider the parties' contested readings of the InterPharm study or the evidence or lack thereof of structural identity.

sion. We therefore reverse the district court's grant of a conditional new trial on anticipation.

CONCLUSION

For the reasons discussed above, we reverse the district court's grant of judgment as a matter of law of no anticipation and the conditional grant of a new trial on anticipation. We remand with instructions to reinstate the jury verdict on anticipation. We need not and do not address the several other issues raised by the parties on appeal.

REVERSED AND REMANDED

APPENDIX B

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

NO. 2019-1133

BIOGEN MA INC.,

Plaintiff-Appellee,

v.

EMD SERONO, INC.,
PFIZER INC.,

Defendants-Appellants,

BAYER HEALTHCARE PHARMACEUTICALS INC.,
NOVARTIS PHARMACEUTICALS CORPORATION

Defendants.

ERRATA

November 20, 2020
Decided: September 28, 2020
Precedential Opinion

Please make the following changes:

On page 8, lines 17-20, change "emphasized that whereas the attached carbohydrate groups in native IFN-β protein were glycosolated, the attached carbohydrate groups in recombinant IFN-β were *not* glycosolated," to —explained that the glycosylation

patterns in native IFN-β and recombinant IFN-β were different,—.

APPENDIX C

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

NO. 2019-1133

BIOGEN MA INC.,

Plaintiff-Appellee,

v.

EMD SERONO, INC.,
PFIZER INC.,

Defendants-Appellants,

BAYER HEALTHCARE PHARMACEUTICALS INC.,
NOVARTIS PHARMACEUTICALS CORPORATION

Defendants.

ERRATA

October 9, 2020
Decided: September 28, 2020
Precedential Opinion

Please make the following change:

On page 18, line 13, change "linear sequence of proteins" to —linear sequence of amino acids—.

APPENDIX D

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

[ORIGINAL OPINION]

No. 2019-1133

BIOGEN MA INC.,

Plaintiff-Appellee,

v.

EMD SERONO, INC.,
PFIZER INC.,

Defendants-Appellants,

BAYER HEALTHCARE PHARMACEUTICALS INC.,
NOVARTIS PHARMACEUTICALS CORPORATION

Defendants.

Appeal from the United States District Court for the District of New Jersey in No. 2:10-cv-02734-CCC-MF, United States District Judge Claire C. Cecchi.

OPINION

September 28, 2020

NICHOLAS P. GROOMBRIDGE, Paul, Weiss, Rifkind, Wharton & Garrison LLP, New York, NY, argued for plaintiff-appellee. Also represented by PETER SANDEL, ERIC ALAN STONE, JENNY CHIA CHENG WU, JOSEPHINE

YOUNG; DAVID J. BALL, JR., Washington, DC; JOHN D. TORTORELLA, KEVIN H. MARINO, Marino Tortorella & Boyle, PC, Chatham, NJ.

MARK ANDREW PERRY, Gibson, Dunn & Crutcher LLP, Washington, DC, argued for defendants-appellants. Also represented by CHRISTINE RANNEY, Denver, CO; WAYNE M. BARSKY, TIMOTHY P. BEST, Los Angeles, CA; JAYSEN CHUNG, San Francisco, CA.

BRUCE GENDERSON, Williams & Connolly LLP, Washington, DC, for amicus curiae Bayer Healthcare Pharmaceuticals Inc. Also represented by DAVID I. BERL, SETH BOWERS, DAVID M. KRINSKY.

Before NEWMAN, LINN, and HUGHES, *Circuit Judges*.

LINN, *Circuit Judge*.

This appeal arises from a suit filed by Biogen MA, Inc. ("Biogen") against EMD Serono, Inc. and Pfizer, Inc. (collectively "Serono") in the District of New Jersey.[1] The suit alleged contributory and induced infringement of Biogen's U.S. Patent Number 7,588,755 ("'755 patent") by the sale and marketing in the United States of Rebif, a recombinant interferon-β ("IFN-β") product used for the treatment of Multiple Sclerosis ("MS"). After a five-week trial, a jury found that the '755 patent claims were anticipated by two references teaching the use of native IFN-β to treat viral diseases: Kingham *et al.*, *Treatment of HBsAg-positive Chronic Active Hepatitis with Hu-*

[1] Biogen also asserted infringement claims against Bayer Healthcare Pharmaceuticals Inc. ("Bayer") and Novartis Pharmaceuticals Corp. ("Novartis"). The actions against Bayer and Novartis were severed from those giving rise to this appeal. Order Granting Bayer's Motion to Sever, Oct. 27, 2017, ECF No. 743. Bayer filed an amicus brief here.

man Fibroblast Interferon, 19(2) Gut 91 (1978) ("Kingham") and Sundmacher *et al.*, *Human Leukocyte and Fibroblast Interferon in a Combination Therapy of Dendritic Keratitis*, 208(4) Albrecht von Graefes Archiv für Klinische & Experimentelle Opthalmologie 229 (1978) ("Sundmacher"). The jury also held the asserted claims not invalid for lack of enablement or written description, or for obviousness. Finally, the jury held that patients and prescribers directly infringed the asserted claims and that Serono contributorily infringed the claims but did not induce infringement thereof.

On cross-motions, the district court granted judgment as a matter of law ("JMOL") of no anticipation in favor of Biogen and conditionally granted a new trial on anticipation. *In re Biogen '755 Patent Litig.*, 335 F. Supp. 3d 688 (D.N.J. 2018) ("*Biogen I*"). The district court also ruled in favor of Biogen: sustaining the jury's verdict of no invalidity based on written description or enablement; overturning the verdict of no induced infringement; sustaining the verdict of contributory infringement; and holding that the '755 patent claims were not patent ineligible. *Id.* Serono appeals the district court's JMOL rulings on anticipation, written description, enablement, contributory infringement, induced infringement and patent eligibility. We have jurisdiction under 28 U.S.C. § 1295(a).

Because a reasonable jury could find the claims of the '755 patent anticipated on the record presented in this case, we reverse the district court's JMOL of no anticipation and its conditional grant of new trial on that ground. We remand with instructions to reinstate the jury verdict of anticipation. We need not and do not address the other grounds asserted on appeal.

I

The '755 patent is directed to a method of treating a viral condition, a viral disease, cancers or tumors, by administration of a pharmaceutically effective amount of a recombinant polypeptide related to human interferon-β ("IFN-β"). The human immune system naturally produces IFN-β in small amounts, and it is undisputed that IFN-β harvested from human cells ("native IFN-β") was used in the prior art to treat viral conditions. See '755 patent, col. 2, l. 53-col. 4, l. 22.

Representative claim 1 of the '755 patent reads:

> 1. A method for immunomodulation or treating a viral condition[ ], a viral disease, cancers or tumors comprising the step of administering to a patient in need of such treatment a therapeutically effective amount of a composition comprising:
>
> a recombinant polypeptide produced by a non-human host transformed by a recombinant DNA molecule comprising a DNA sequence selected from the group consisting of:
>
> (a) DNA sequences which are capable of hybridizing to any of the DNA inserts of G-pBR322(Pst)/HFIF1, G-pBR322(Pst)/HFIF3 (DSM 1791), G-pBR322(Pst)/HFIF6 (DSM 1792), and GpBR322(Pst)/HFIF7 (DSM 1793) under hybridizing conditions of 0.75 M NaCl at 68° C. and washing conditions of 0.3 M NaCl at 68° C., and which code for a polypeptide displaying antiviral activity, and
>
> (b) DNA sequences which are degenerate as a result of the genetic code to the DNA sequences defined in (a);

> said DNA sequence being operatively linked to an expression control sequence in the recombinant DNA molecule.

'755 patent, col. 49, l. 59-col. 50, l. 12. Dependent claim 2 replaces the "capable of hybridizing" limitation with a selection from two particular DNA sequences, one of which is the DNA sequence of human interferon-beta. *Id.* at col. 50, ll. 13-52. Claims 1 and 2 thus define the claimed polypeptide by reference to the DNA sequence inserted into the host during the recombinant manufacture of the polypeptide. Claim 3, dependent from claim 1, limits the polypeptide to a particular linear polypeptide sequence. Because the claimed IFN-β DNA and polypeptide sequences are derived from human IFN-β, it is indisputable that native human IFN-β is capable of hybridizing with the DNA sequences in claim 1, is produced by one of the DNA sequences laid out in claim 2, and comprises the amino acid sequence set out in claim 3. See J.A. 47784 (Fiers Aff. To the Canadian Patent Office, indicating that the recombinant IFN-β was derived from human IFN-β cDNA); J.A. 77897 (Dr. Green Test., testifying that the sequences claimed in claim 1 are "DNA that will hybridize to one of the four human beta interferon clones"); J.A. 77904 (Dr. Green Test., testifying that accused-product Rebif is capable of hybridizing to one or more of the DNA inserts because the DNA sequence it used is identical to the published sequence of human IFN-β). For purposes of this opinion, we refer to "recombinant IFN-β" as shorthand for the recombinant protein that meets these claim limitations.

During *Markman*, the district court held that claim 1 covers a "one-step method of 'administering' to a patient in need the specified recombinant HuIFN-β." Markman Opinion at 17, Mar. 28, 2016, ECF No. 403. The district

court considered the claimed "produced" and "transformed" steps "merely descriptive of the recombinant polypeptide to be administered," i.e. merely source limitations. *Id.* at 15. The district court also held that it was "unclear that [the] method of treatment claim can be treated as a product-by-process claim," and that it was "aware of no binding precedent requiring method of treatment claims to be treated as product-by-process claims in the claim construction context." *Id.* at 14. The district court did not construe "polypeptide," "therapeutically effective amount," or "antiviral activity," and neither party asked the court to consider whether the claims covered the linear sequence of amino acids or the three-dimensional structure of the protein.

Biogen, Serono, and Bayer all moved for summary judgment. Before Bayer was severed, Bayer argued that it was entitled to summary judgment of anticipation because the claimed recombinant IFN-β and the prior art native IFN-β shared the same linear amino acid sequence. The district court denied Bayer's motion, holding, *inter alia*, that the claims require the polypeptide to have "antiviral activity" and be administered in a "therapeutically effective amount." Summary Judgment Opinion at 28, Jan. 9, 2018, ECF No. 892. The district court concluded that those requirements necessitate that the polypeptide "be folded into its appropriate three-dimensional structure," and that Bayer was therefore not entitled to summary judgment of anticipation by merely showing that the amino acid sequence of recombinant IFN-β and the amino acid sequence of native IFN-β were identical. *Id.*

After a five-week trial, Biogen and Serono both moved for JMOL under Federal Rule of Civil Procedure 50(a). The district court deferred ruling until the jury verdict.

Among other issues, the court submitted anticipation, obviousness, enablement, written description, and contributory and induced infringement to the jury. In its charge on anticipation, the district court told the jury that "[t]he term 'polypeptide' means 'a linear array of amino acids connected one to the other by peptide bonds between the αamino and carboxy groups of adjacent amino acids,'" and that the jury "must accept my definition of these words in the claims as correct." Final Jury Instructions at 17, Feb. 21, 2018, ECF No. 968. Biogen did not object to these instructions and did not request any instruction defining the polypeptide in terms of its three-dimensional structure or requiring identity of the three-dimensional structures of native IFN-β and recombinant IFN-β proteins to establish anticipation.

The jury held, *inter alia*, that all claims in the '755 patent were invalid as anticipated by native IFN-β; not invalid for obviousness, lack of enablement or lack of written description; and that Serono was liable for contributory infringement but not induced infringement. Jury Verdict Form at 1-6, Feb. 23, 2018, ECF No. 977.

Both parties renewed their JMOL motions. As relevant here, the district court granted Biogen's motion of no anticipation as a matter of law. *Biogen I*, 335 F. Supp. 3d at 713. In a comprehensive opinion, the district court held that no reasonable jury could find anticipation under Serono's reading of the claims. First, applying a structural reading of the recombinant limitations, the district court held that Serono had not identified any prior art that disclosed "treatment with a 'therapeutically effective amount' of a composition comprising a 'recombinant' interferon-β polypeptide produced in a 'non-human host' that had been 'transformed by a recombinant DNA molecule.'" *Id.* at 704. **[JA21]**. The district court reasoned

that because treatment in the prior art entailed administration of native IFN-β, which was undisputedly not recombinantly produced, no reasonable jury could find anticipation. *Id.* at 705. The district court cited but did not distinguish *Amgen Inc.* v. *Hoffman-La Roche Ltd.*, 580 F.3d 1340 (Fed. Cir. 2009), which analyzed anticipation of a claimed recombinant erythropoietin ("EPO") by prior art urinary (i.e. natural) EPO. *Biogen I*, 335 F. Supp. 3d at 1367. The district court declined to apply a product-by-process analysis to a product-by-process limitation contained within a method of treatment claim, concluding that no precedent required such an analysis and that the policy informing product-by-process claims—to enable an inventor to claim an otherwise difficult-to-define product—was inapplicable to the instant method of treatment claims. *Id.* at 712-13.

In the alternative, the district court held that no reasonable jury could have found anticipation even applying a product-by-process analysis. *Id.* at 705-11. The district court explained that because the claims required administration of a "therapeutically effective amount" of a recombinant polypeptide that "displays antiviral activity," the product resulting from the claimed recombinant process is defined by the folded three-dimensional structure of the protein. *Id.* at 705 (discussing Summary Judgment Opinion at 28, Jan. 9, 2018, ECF No. 892). The district court held that the jury lacked substantial evidence that the native IFN-β protein as disclosed in Kingham and Sundmacher was structurally or functionally identical to the claimed three-dimensional recombinant IFN-β protein. *Id.*

With respect to structural identity, the district court emphasized that whereas the attached carbohydrate groups in native IFN-β protein were glycosolated, the

attached carbohydrate groups in recombinant IFN-β were *not* glycosolated, and that this change affected the three-dimensional structure of the protein. *Id.* The district court—relying on expert testimony by Serono's expert, Dr. Lodish, and statements found in a post-priority date reference created by InterPharm Laboratories Ltd. entitled "Comparative Biochemical Analysis of Native Human Fibroblast lnterferon and Recombinant Beta Interferon Expressed by Chinese Hamster Ovary Cells" ("InterPharm")—concluded that native and recombinant IFN-β were not *identical* but merely very similar. *Id.* at 706-07. The district court opined that the structural differences alone preclude anticipation. *Id.* at 710-11 (relying primarily on this court's decision in *Amgen*, 580 F.3d at 1367-69, in which we affirmed a holding of no anticipation based on structural differences). Finally, the district court discounted the conclusion in the InterPharm study that recombinant IFN-β and native IFN-β were identical. It held that there was no substantial evidence that the generic "native IFN-β" analyzed in the InterPharm study and found to be identical to recombinant IFN-β was the same native IFN-β taught in the prior art. *Id.* at 708.

As for functional identity, the district court held that the relative ease of manufacture of recombinant IFN-β in large quantities functionally distinguished it from native IFN-β. *Id.* at 709-10.

For these reasons, the district court granted JMOL of no anticipation. *Id.* at 713. The district court also conditionally granted Biogen's motion for a new trial on anticipation "[f]or the same reasons the Court grants Biogen's JMOL motion." *Id.* The district court added that the trial was complex and was "noticeably focused on issues

other than anticipation," such that that the jury verdict deserved close scrutiny. *Id.*

Serono appeals. We have jurisdiction under 28 U.S.C. § 1295.

II

We review the grant of JMOL and the grant of new trial under the law of the regional circuit. *Uniloc USA, Inc.* v. *Microsoft Corp.*, 632 F.3d 1292, 1301, 1309 (Fed. Cir. 2011). The Third Circuit reviews the grant of JMOL for a fact question de novo, affirming "only if, viewing the evidence in the light most favorable to the nonmovant and giving it the advantage of every fair and reasonable inference, there is insufficient evidence from which a jury reasonably could find liability." *Lightning Lube, Inc.* v. *Witco Corp.*, 4 F.3d 1153, 1166-67 (3d Cir. 1993); *Garzier ex rel. White* v. *City of Phila.*, 328 F.3d 120, 123 (3d Cir. 2003) ("A district court should grant such a motion only if, viewing all the evidence in favor of the nonmoving party, no reasonable jury could find liability on a particular point."). The Third Circuit reviews the conditional grant of a new trial against the weight of the evidence for an abuse of discretion, "unless the court's denial is based on the application of a legal precept, in which case the standard of review is plenary." *Lightning Lube*, 4 F.3d at 1167.

III

A claim is anticipated only if "each and every [limitation] is found within a single prior art reference." *Summit 6, LLC* v. *Samsung Elecs. Co.*, 802 F.3d 1283, 1294 (Fed. Cir. 2015). Anticipation is a factual question and thus within the ordinary provenance of the jury. *Lighting Ballast Control LLC* v. *Phillips Elecs. N. Am. Corp.*, 790 F.3d 1329, 1340 (Fed. Cir. 2015).

In evaluating the evidentiary record presented to the jury on the question of anticipation, the district court: (1) declined to apply a product-by-process analysis to the claimed recombinant IFN-β source limitation; and (2) in its alternative ground analysis, required identity of three-dimensional structures not specifically recited in the claims rather than the claimed and lexicographically defined "polypeptide." Both of these determinations led to an erroneous conclusion on anticipation.

A. The Recombinant Source of the Polypeptide

The district court, focusing on the process of making recombinant IFN-β, concluded that it need not analyze whether native IFN-β and recombinantly produced IFN-β were identical because neither Kingham nor Sundmacher prior art reference taught a method of treatment *using recombinant IFN-β*. *Biogen I*, 335 F. Supp. 3d at 704. It categorized the "produced" and "transformed" limitations as meaningful "source limitations." *Id.* at 711-12. The district court was convinced that because the recombinant source limitations here overcame the shortcoming of the prior art—namely, the unavailability of native IFN-β in sufficient quantity to facilitate practical treatment—the recombinant nature of the claimed IFN-β "lies at the heart of the benefit of this invention" [and] should be given "force and effect in the anticipation analysis.'" *Id.* (quoting Biogen's statements at JMOL hearing, Trial Tr. 6/6/18 at 12:7-10). The district court reasoned that no binding precedent required it to apply a product-by-process analysis to a limitation contained in a method of treatment claim, and held that the rationale underlying the use of product-by-process claims—to allow claiming of an otherwise difficult-to-define invention, see *SmithKline*, 439 F.3d at 1315—did not apply to the claims here because the "product" itself was sufficiently

described. *Biogen I*, 335 F. Supp. 3d. at 713. The district court thus concluded there could be no anticipation, regardless of whether Serono had shown the identity of native IFN-β and recombinant INF-β.

Serono contends that Biogen has waived any argument that the recombinant source of the IFN-β can alone confer novelty because Biogen's pre-verdict JMOL motion only argued that native IFN-β and recombinant IFN-β were not identical. We find no waiver. The source limitation was one of the bases for Biogen's argument of non-identity and was considered by the district court at Summary Judgment and in its opinion on JMOL.

On the merits, Serono asserts that a source limitation alone cannot confer novelty unless the product itself is novel. Serono argues that the district court erred by holding that the lack of a recombinantly produced IFN-β product in the prior art compelled a finding of no anticipation. Biogen argues that the source of the IFN-β matters is an independent limitation.

We agree with Serono. The district court's refusal to consider the identity of recombinant and native IFN-β runs afoul of the longstanding rule that "an old product is not patentable even if it is made by a new process." *Amgen*, 580 F.3d at 1366. See also *Gen. Elec. Co.* v. *Wabash Appliance Corp.*, 304 U.S. 364, 373 (1938) ("[A] patentee who does not distinguish his product from what is old except by reference, express or constructive, to the process by which he produced it, cannot secure a monopoly on the product by whatever means produced."); *Cochrane* v. *Badische Anilin & Soda Fabrik*, 111 U.S. 293, 311 (1884) ("While a new process for producing [an old product] was patentable, the product itself could not be patented, even though it was a product made artificially for the first time."); *SmithKline Beecham Corp.* v.

Apotex Corp., 439 F.3d 1312, 1317 (Fed. Cir. 2006) ("It has long been established that one cannot avoid anticipation by an earlier product disclosure by claiming the same product . . . as produced by a particular process.").

In *Amgen*, we explained that a claim to a recombinant EPO composition must be analyzed for novelty by comparing the recombinant EPO to the prior art urinary EPO. We further explained that simply because prior art urinary EPO was not made recombinantly was not enough to avoid anticipation as a matter of law.[2] 580 F.3d at 1370 ("To prove invalidity, Roche had to show that recombinant EPO was the same as urinary EPO, *even though urinary EPO was not made recombinantly*.") (emphasis added). The key question was "whether the production of EPO by recombinant technology resulted in a new product," *id.* at 1367, or, "[i]n other words, does the source limitation 'purified from mammalian cells grown in culture' distinguish recombinant EPO from [prior art] urinary EPO?" *Id.*

The nature of the origin or source of the composition recited in the claims at issue in this case is, in all relevant respects, identical to that considered in *Amgen*. As in *Amgen*, the recombinant origin of the recited composi-

---

[2] The key claim in *Amgen* read: "A pharmaceutical composition comprising a therapeutically effective amount of human erythropoietin and a pharmaceutically acceptable diluent, adjuvant or carrier, wherein said erythropoietin is purified from mammalian cells grown in culture." 580 F.3d at 1364. An additional independent claim in a related patent read: "A non-naturally occurring glycoprotein product of the expression in a mammalian host cell of an exogenous DNA sequence comprising a DNA sequence encoding human erythropoietin said product possessing the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells." *Id.* In relevant part, we applied the same analysis to both claims.

tion cannot alone confer novelty on that composition if the product itself is identical to the prior art non-recombinant product. The requirements that the claimed polypeptide is "recombinant" and "produced by a non-human host transformed by a recombinant DNA molecule" (in the case of Claim 1 of the '755 patent) describe the process by which the product, i.e. the "polypeptide," is formed. These are not additional structural limitations. See *Purdue Pharma L.P.* v. *Epic Pharma, LLC*, 811 F.3d 1345, 1353 (Fed. Cir. 2016) (holding that because a source limitation of a composition "has no effect on its structure . . . [that] limitation . . . cannot be a structural limitation"). The key question for anticipation here, as in *Amgen*, is thus whether the recombinant *product* is identical to the prior art *product*—not whether the prior art product was made recombinantly.

Biogen argues that *Amgen* is limited to composition claims and is not applicable to the method of treatment claims at issue here. To support this proposition, Biogen relies on general statements in product-by-process cases such as *In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985) (applying product-by-process analysis for "an otherwise patentable *product*") (emphasis added), and the well-recognized distinction patent law draws between the scope of composition and method of treatment claims. See, *e.g.*, *Ass'n for Molecular Pathology* v. *Myriad Genetics, Inc.*, 569 U.S. 576, 595 (2013) (recognizing the distinct scope for composition and method of treatment claims in the context of 35 U.S.C. § 101).

Biogen's only basis for novelty of the method of treatment claims at issue here is the novelty of the recombinant IFN-β composition that is administered. That composition is claimed in terms of the process by which it is manufactured. If the novelty of the recombinant IFN-β

composition requires comparing its structure to the structure of native IFN-β, as *Amgen* requires, it would defy all reason to excuse that analysis for a method of administration claim using that composition. Such a rule could have the absurd result that a recombinant composition could be non-novel, the method of administration could be non-novel, but the method of administration of the composition defined by the process of its manufacture would be novel as a matter of law.

There is no logical reason why the nesting of a product-by-process limitation within a method of treatment claim should change how novelty of that limitation is evaluated. Indeed, we have previously applied product-by-process analysis to a nested limitation. In *Purdue Pharma*, we interpreted a claim to "an oral dosage form comprising . . . oxycodone hydrochloride active pharmaceutical ingredient having less than 25 ppm 14-hydroxy[ ], wherein at least a portion of the 14-hydroxy [ ] is derived from 8α[ ] during conversion of oxycodone free base to oxycodone hydrochloride" as including a product-by-process limitation; namely, the 14-hydroxy as derived. *Purdue Pharma*, 811 F.3d at 1353 (emphasis omitted). Similar to our analysis here, the court in *Purdue Pharma* held that it was appropriate to focus on the identity of the products of the claimed and prior art processes, and not on the source limitation, in analyzing obviousness. See *id.* at 1353-54. The nesting of the product-by-process limitation within a method of treatment claim does not change the proper construction of the product-by-process limitation itself.

We are also unpersuaded by the district court's and Biogen's reasoning that a product-by-process-type analysis is inappropriate here because the composition was otherwise capable of definition other than by the process.

That argument is precluded by *Amgen*, where the product was also well-defined in the claims: "human erythropoietin . . . wherein said erythropoietin is purified from mammalian cells grown in culture." 580 F.3d at 1364. Furthermore, as noted *supra*, the rule in *Amgen* is a necessary outgrowth of the black-letter legal principle that an old product made by a new process is not novel and cannot be patented. Logic compels extending that rule to the present case; an old method of administration of an old product made by a new process is not novel and cannot be patented.

Biogen is certainly correct that the scope of composition and method of treatment claims is generally subject to distinctly different analyses. But where, as here, the novelty of the method of administration rests wholly on the novelty of the composition administered, which in turn rests on the novelty of the source limitation, the *Amgen* analysis will necessarily result in the same conclusion on anticipation for both forms of claims.

Finally, the district court erred in considering the advantages of the *recombinant process*—the new capability of manufacturing sufficient quantities of IFN-β through recombinant technology—as a reason not to apply a product-by-process analysis. See *Biogen I*, 335 F. Supp. 3d at 713. That consideration may well be relevant in considering the novelty of the recombinant *process*, but, a new process, regardless of its novelty, does not make an old product created by that process novel. This does not fail to give "force and effect" to the heart of the claimed invention; it protects the public from attempts to excise old products from the public domain.

Because a proper anticipation analysis of the claims in the '755 patent turns not on the source of the claimed polypeptide but on a comparison of the claimed recombi-

nant polypeptide and the prior art native polypeptide, the district court erred in concluding that the mere absence of recombinantly produced IFN-β in the prior art was sufficient to grant JMOL of no anticipation.

B. The Three-Dimensional Structure of the Polypeptide

The district court also held that even applying a product-by-process type analysis, no reasonable jury could have found anticipation because the jury lacked sufficient evidence of identity between the claimed recombinant "polypeptide" and the native IFN-β. In particular, the district court concluded that just because recombinant and native IFN-β "share the same linear amino acid sequence is not enough for purposes of anticipation." *Id.* at 705. The district court took the position that native polypeptide anticipates the "recombinant polypeptide" only if their respective folded three-dimensional proteins share identical structure and function. *Id.* The district court reasoned that without a disclosure in the prior art of such three-dimensional protein, a showing of the native polypeptide alone would not necessarily produce "antiviral activity" when administered in a "therapeutically effective amount" as recited in the claims. *Id.* (citing Summary Judgment Opinion at 28, ECF No. 892). This was error.

The "product" administered in the claimed method is the "polypeptide." See '755 patent, col. 49, ll. 59-64 ("A method . . . comprising the step of administering . . . a therapeutically effective amount of a composition comprising: a recombinant polypeptide produced by a non-human host . . . ."). As noted *supra*, the key question for anticipation is whether the native "polypeptide" is identical to the "polypeptide" "produced by" the recited recombinant process.

Biogen explicitly defined "polypeptide" in the '755 patent:

> Polypeptide—A linear array of amino acids connected one to the other by peptide bonds between the α-amino and carboxy groups of adjacent amino acids.

'755 patent, col. 8, ll. 62-64. The "polypeptide" structure is thus defined by reference to its "linear" array, without regard to its folded protein structure. The district court charged the jury with this definition, adding that the jury "must accept my definition of these words in the claims as correct." Final Jury Instructions at 17, ECF No. 968. Biogen did not object to this charge and did not ask the court for a jury instruction requiring identity of the folded protein structures.

As the district court recognized on summary judgment, "Biogen does not dispute that '[t]he sequential order of the amino acid residues for native IFN-β is the same as the sequential order of the amino acid residues for recombinant IFN-β.'" Summary Judgment Opinion at 27, ECF No. 892. See also Biogen Brief at 19. Thus, the native IFN-β polypeptide and the claimed recombinant IFN-β polypeptide are identical for purposes of the instant claim.

Biogen argues that the district court was correct in requiring identity not just of the polypeptide, but also of the folded proteins, because the claims require the administration of "*a therapeutically effective amount* of a composition" and that the DNA sequences in the claims must "code for a polypeptide displaying *antiviral activity*." Biogen asserts that only three-dimensional proteins can be therapeutically effective and have antiviral activity, and therefore that the "product" to be analyzed for

novelty is the folded three-dimensional protein, not just the amino acid sequence.

Biogen is incorrect. First, Biogen's argument fails to give effect to Biogen's explicit definition of "polypeptide" in the specification. We must respect this lexicographic choice. See *Edward Lifesciences LLC* v. *Cook Inc.*, 582 F.3d 1322, 1329 (Fed. Cir. 2009) ("[W]e will adopt a definition that is different from the ordinary meaning when 'the patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in . . . the specification'" (quoting *CCS Fitness, Inc.* v. *Brunswick Corp.*, 288 F.3d 1359, 1366-67 (Fed. Cir. 2002))). Biogen does not attempt to square its theory with the definition in the specification.

Second, Biogen draws the wrong conclusion from the claimed antiviral activity limitation. The claims, in calling for antiviral activity, do not recite any specific folded three-dimensional structure that gives rise to that activity. While it is indisputable that an amino acid sequence alone cannot give rise to antiviral activity, it is also indisputable that every linear sequence of proteins will fold into *some* three-dimensional configuration. The claimed antiviral activity can arise from the administration of any three-dimensional protein with a linear amino acid sequence identical to the claimed recombinant "polypeptide."

Finally, and importantly, Biogen did not ask for a jury instruction on anticipation that required comparing the three-dimensional protein structures of prior art IFN-β and the claimed recombinant IFN-β. Neither Biogen nor the district court can reframe the anticipation inquiry on JMOL to focus on the unclaimed three-dimensional protein structure, where the jury was instructed, without objection, to decide anticipation based on the linear ami-

no acid sequence. See *Finjan, Inc.* v. *Blue Coat Sys., Inc.*, 879 F.3d 1299, 1306 (Fed. Cir. 2018) ("[I]t is too late at the JMOL stage to . . . adopt a new and more detailed interpretation of the claim language and test the jury verdict by that new and more detailed interpretation." (quoting *Hewlett-Packard Co.* v. *Mustek Sys., Inc.*, 340 F.3d 1314, 1321 (Fed. Cir. 2003))).

The jury was correctly instructed that "to be entitled to a patent, the invention must actually be 'new.'" J.A. 81262. It is undisputed that the prior art here teaches the administration of native IFN-β that has a linear amino acid sequence identical to the linear amino acid sequence of the recited recombinant IFN-β and that shows antiviral activity. See '755 patent, col. 3, ll. 4-14. The jury thus had sufficient evidence to find that native IFN-β polypeptide is identical to recombinant IFN-β polypeptide, was administered in therapeutically effective amounts, and showed antiviral activity in the prior art. The district court thus erred in granting JMOL of no anticipation.[3]

IV. CONDITIONAL GRANT OF NEW TRIAL

The district court also conditionally granted a new trial on anticipation. The district court's grant of a new trial was based on the same legal errors supporting its grant of JMOL. *Biogen I*, 335 F. Supp. 3d at 713 ("For the same reasons the Court grants Biogen's JMOL motion, the Court conditionally orders a new trial on anticipation."). None of the additional considerations noted by the district court in support of its conditional grant of a

[3] Because the proper construction of the claims does not require comparison of the three-dimensional structure of prior art native IFN-β and recombinant IFN-β, we need not consider the parties' contested readings of the InterPharm study or the evidence or lack thereof of structural identity.

new trial are independently sufficient to support its decision. We therefore reverse the district court's grant of a conditional new trial on anticipation.

CONCLUSION

For the reasons discussed above, we reverse the district court's grant of judgment as a matter of law of no anticipation and the conditional grant of a new trial on anticipation. We remand with instructions to reinstate the jury verdict on anticipation. We need not and do not address the several other issues raised by the parties on appeal.

REVERSED AND REMANDED

APPENDIX E

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

CIVIL ACTION NO.: 10-2734 (CCC)(MF)
(CONSOLIDATED)

IN RE BIOGEN '755 PATENT LITIGATION

OPINION

September 7, 2018

CECCHI, District Judge.

The Court held a five-week jury trial in this patent infringement action beginning on January 18, 2018. On February 23, 2018, the jury returned a verdict finding that healthcare professionals and/or patients directly infringe claims 1 and 2 of United States Patent No. 7,588,755 (the "'755 patent") when they administer or self-administer the product Rebif® for the treatment of multiple sclerosis ("MS"), that Defendants EMD Serono, Inc. ("Serono") and Pfizer Inc. ("Pfizer") (collectively, "Defendants") have contributed to the infringement of claims 1 and 2 by selling or offering to sell Rebif®, that neither Serono nor Pfizer has actively induced the infringement of claims 1 or 2, that claims 1, 2, and 3 of the '755 patent are not invalid for obviousness, lack of adequate written description, or lack of enablement, and that claims 1, 2, and 3 are invalid for anticipation. ECF No. 977 ("Verdict Form").

Now pending before the Court are renewed motions for judgment as a matter of law ("JMOL") pursuant to Federal Rule of Civil Procedure 50(b) by Plaintiff Biogen MA Inc. ("Biogen") and Defendants. ECF Nos. 980, 982. Specifically, Biogen moves for JMOL on the issues of anticipation, induced infringement by Serono and Pfizer, certain defenses that were not litigated at trial, and certain subsidiary damages-related issues. Biogen also moves conditionally and in the alternative for a new trial as to certain issues pursuant to Federal Rules of Civil Procedure 50(c) and 59, respectively. Defendants move for JMOL on the issues of patent eligibility, obviousness, enablement, written description, contributory infringement by Pfizer, and lost profits damages.

The Court heard oral argument on June 6, 2018. The parties also submitted letters following oral argument. ECF Nos. 1010, 1011, 1012, 1014, 1015, 1017, 1018. Having considered the parties' written submissions and oral presentations, and for the reasons discussed below, Biogen's JMOL motions with respect to anticipation, induced infringement against Serono and Pfizer, and certain non-litigated defenses are hereby **GRANTED**. The Court also conditionally orders a new trial on anticipation and induced infringement against Serono and Pfizer pursuant to Rule 50(c), and orders a new trial on all damages issues pursuant to Rule 59. Biogen's remaining JMOL motions and each of Defendants' JMOL motions are hereby **DENIED**.

I. BACKGROUND

On May 28, 2010, Biogen filed this patent infringement suit asserting claims of the '755 patent against Defendants, Bayer HealthCare Pharmaceuticals Inc. ("Bayer"), and Novartis Pharmaceuticals Corp. ("Novartis"). C.A. No. 10-2760, ECF No. 1 ("Compl."). Prior to trial, Bio-

gen's infringement claims against Serono and Pfizer were severed from Biogen's infringement claims against Bayer and Novartis.[1] ECF No. 743. Thus, only Biogen's claims against Serono and Pfizer (and Serono and Pfizer's defenses thereto) were tried before the jury and are the subject of the instant motions.

The '755 patent claims a method for immunomodulation, or treating viral diseases, cancers, or tumors, by administering to a patient a recombinant polypeptide—human interferon beta[2]—that is produced by a non-human host transformed by a recombinant DNA molecule. The '755 patent includes three claims, of which only claim 1 is independent.[3]

Claim 1 of the '755 patent recites:

> 1. A method for immunomodulation or treating a viral conditions [*sic*], a viral disease, cancers or tumors comprising the step of administering to a patient in need of such treatment a therapeuti-

---

[1] Biogen's infringement claims against Bayer and Novartis are based on the sale of products Betaseron® and Extavia® in the United States for the treatment of MS. Compl. ¶¶ 50-73; C.A. No. 10-2760, ECF No. 61 ("Am. Compl.") ¶¶ 60-83. The day before Biogen filed its lawsuit, on May 27, 2010, Bayer sued Biogen seeking a declaration that Bayer does not infringe the '755 patent claims and that the '755 patent claims are invalid. ECF No. 1. On October 1, 2010, Bayer's declaratory judgment action and Biogen's patent infringement suit were consolidated under Civil Action No. 10-2734. ECF No. 37. On October 27, 2017, this Court granted Bayer's and Defendants' motions to sever Biogen's claims against Serono and Pfizer from Biogen's claims against Bayer and Novartis. ECF No. 743.

[2] This Opinion refers to human interferon beta as "interferon-β," "IFN-β," "beta interferon," "fibroblast interferon," "HuIFN-β," and/or "HFIF."

[3] Claims 2 and 3 depend from claim 1 and are also method claims. The parties' motions and this Opinion focus on claim 1.

cally effective amount of a composition comprising:

a recombinant polypeptide produced by a non-human host transformed by a recombinant DNA molecule comprising a DNA sequence selected from the group consisting of:

(a) DNA sequences which are capable of hybridizing to any of the DNA inserts of GpBR322-(Pst)/HFIFI, GpBR322(Pst)/HFIF3 (DSM 1791), G-pBR322(Pst)/HFIF6 (DSM 1792), and GpBR322(Pst)/HFIF7 (DSM 1793) under hybridizing conditions of 0.75 M NaCl at 68∞ C. and washing conditions of 0.3 M NaCl at 68∞ C., and which code for a polypeptide displaying antiviral activity, and

(b) DNA sequences which are degenerate as a result of the genetic code to the DNA sequences defined in (a);

said DNA sequence being operatively linked to an expression control sequence in the recombinant DNA molecule.

The Court previously construed claim 1 of the '755 patent as reciting a "one-step method of 'administering' to a patient in need the specified recombinant HuIFN-β." ECF No. 403 ("*Markman* Op.") at 17. The Court also determined that the "produced" and "transformed" limitations of claim 1 are "merely descriptive of the recombinant polypeptide to be administered" as opposed to separate steps that must be shown to prove infringement. *Id.* at 14-15.

Biogen's infringement claims against Serono and Pfizer are based on the sale of recombinant interferon-β product Rebif® in the United States for the treatment of MS. Compl. ¶¶32-49; Am. Compl. ¶¶42-59. In their An-

swers, Defendants assert that the '755 patent claims are invalid, not infringed, and/or unenforceable. C.A. No. 10-2760, ECF Nos. 56, 57, 75; ECF Nos. 44, 71. The issues of infringement, validity, and damages were tried to a jury for a number of weeks in January and February of 2018.[4] With respect to infringement, the jury was asked to decide whether Serono and Pfizer were each liable for induced and contributory infringement of claims 1 and 2 of the '755 patent (the "asserted claims"). With respect to validity, the jury was asked to decide whether claims 1, 2, and 3 were invalid for obviousness, lack of adequate written description, lack of enablement, or anticipation. Before the case was submitted to the jury, Biogen and Defendants each moved for JMOL on a number of issues pursuant to Federal Rule of Civil Procedure 50(a).[5] 2/9/18 Tr. at 168:21-169:15, 170:18-171:8, 172:4-18, 179:7-23; 2/21/18 Tr. at 20:23-22:3, 52:9-53:24, 62:23-64:5, 67:19-69:16. The Court reserved decision on all of the parties' Rule 50(a) motions. 2/9/18 Tr. at 183:11-12; 2/21/18 Tr. at 75:26-77:4.

On February 23, 2018, the jury returned a verdict finding that healthcare professionals and/or patients directly infringe the asserted claims of the '755 patent when they administer or self-administer Rebif® for the treatment of MS. Verdict Form at 1, Q. 1. The jury also found that neither Serono nor Pfizer has actively induced the direct infringement of the asserted claims. *Id.* at 2-3,

---

[4] Defendants withdrew their inequitable conduct defense at the beginning of the trial. ECF No. 941.

[5] A Rule 50(a) JMOL motion "may be made at any time before the case is submitted to the jury." Fed. R. Civ. P. 50(a)(2). So long as the motion was made during trial, a party may submit a renewed motion for JMOL after the trial. See Fed. R. Civ. P. 50(b); *Rinehimer* v. *Cemcolift, Inc.*, 292 F.3d 375, 383 (3d Cir. 2002).

Qs. 2, 6. The jury further found that both Serono and Pfizer have contributed to the direct infringement of the asserted claims by selling or offering to sell Rebif® in the United States. *Id.* at 3, Qs. 7, 8. With respect to validity, although the jury found that the '755 patent claims were not invalid for obviousness, lack of adequate written description, or lack of enablement, (*id.* at 3-4, Qs. 9-11), it found that the claims were anticipated by prior-art uses of naturally-occurring (or native), human interferon-β (*id.* at 4, Q. 12). Accordingly, the jury did not reach the issue of damages, leaving the damages questions on the Verdict Form blank. *Id.* at 5-6, Qs. 13-18.

Following the verdict, on March 16, 2018 the Court held a telephone conference with the parties to discuss a schedule for filing post-trial motions pursuant to Rule 50(b). In its Rule 50(b) JMOL motions, Biogen asks the Court to enter judgment that the '755 patent claims are not anticipated by prior-art uses of native, human interferon-β and that Serono and Pfizer have each induced infringement of the asserted claims. ECF No. 980-1 ("Biogen Br."). Biogen also seeks a judgment in its favor on certain damages-related issues and as to certain non-litigated defenses. Biogen further asks the Court to conditionally grant a new trial under Rule 50(c) for each of those issues except for the non-litigated defenses, and alternatively moves for a new trial under Rule 59 for any of those issues on which the Court does not grant JMOL. Defendants oppose each of Biogen's motions. ECF No. 991 ("Defs. Opp."). In their Rule 50(b) JMOL motions, Defendants ask the Court to enter judgment that Pfizer has not contributed to the infringement of the asserted claims, that the '755 patent claims are patent ineligible, that the '755 patent claims are invalid on the grounds of obviousness, lack of enablement, and lack of adequate

written description, and that Biogen is not entitled to lost profits damages. ECF No. 983 ("Defs. Br."). Biogen opposes each of Defendants' motions. ECF No. 989 ("Biogen Opp."). The Court heard oral argument on June 6, 2018 ("6/6/18 Tr.").

II. Legal Standards

A. Motion for Judgment as a Matter of Law

Judgment as a matter of law is appropriate if "the court finds that a reasonable jury would not have a legally sufficient evidentiary basis to find for [a] party" on an issue. Fed. R. Civ. P. 50(a)(1). "If the court does not grant a motion for judgment as a matter of law made under Rule 50(a), the court is considered to have submitted the action to the jury subject to the court's later deciding the legal questions raised by the motion." Fed. R. Civ. P. 50(b). In ruling on a Rule 50(b) motion, "the court may: (1) allow judgment on the verdict, if the jury returned a verdict; (2) order a new trial; or (3) direct the entry of judgment as a matter of law." *Id.*

To prevail on a renewed motion for JMOL under Rule 50(b) following a jury trial and verdict, the moving party "must show that the jury's findings, presumed or express, are not supported by substantial evidence or, if they were, that the legal conclusion(s) implied by the jury's verdict cannot in law be supported by those findings." *Power Integrations, Inc.* v. *Fairchild Semiconductor Int'l, Inc.*, 843 F.3d 1315, 1326 (Fed. Cir. 2016) (quoting *Pannu* v. *Iolab Corp.*, 155 F.3d 1344, 1348 (Fed. Cir. 1998)). "Substantial evidence" is defined as "such relevant evidence from the record taken as a whole as might be accepted by a reasonable mind as adequate to support the finding under review." *Perkin-Elmer Corp.* v. *Computervision Corp.*, 732 F.2d 888, 893 (Fed. Cir. 1984) (citations omitted).

In the Third Circuit, JMOL "should be granted only if, viewing the evidence in the light most favorable to the nonmovant and giving it the advantage of very fair and reasonable inference, there is insufficient evidence from which a jury reasonably could find" for the nonmovant. *Lightning Lube, Inc.* v. *Witco Corp.*, 4 F.3d 1153, 1166 (3d Cir. 1993) (citing *Wittekamp* v. *Gulf & Western Inc.*, 991 F.2d 1137, 1141 (3d Cir. 1993)). "The question is not whether there is literally no evidence supporting the party against whom the motion is directed but whether there is evidence upon which the jury could properly find a verdict for that party." *Id.* (quoting *Patzig* v. *O'Neil*, 577 F.2d 841, 46 (3d Cir. 1978)). The district court "may not weigh the evidence, determine the credibility of witnesses, or substitute its version of the facts for the jury's version." *Id.* (citation omitted). While JMOL motions should be granted sparingly, "a scintilla of evidence is not enough to sustain a verdict of liability." *Id.* (citing *Walter* v. *Holiday Inns, Inc.*, 985 F.2d 1232, 1238 (3d Cir. 1993)). Moreover, "although the court should review the record as a whole, it must disregard all evidence favorable to the moving party that the jury is not required to believe." *Reeves* v. *Sanderson Plumbing Prods., Inc.*, 530 U.S. 133, 151, 120 S.Ct. 2097, 147 L.Ed.2d 105 (2000) (citing 9A C. Wright & A. Miller, Federal Practice and Procedure §2529, p. 299 (2d ed. 1995)); *Integra Lifesciences I, Ltd.* v. *Merck KGaA*, 496 F.3d 1334, 1345 (Fed. Cir. 2007). "That is, the court should give credence to the evidence favoring the nonmovant as well as that evidence supporting the moving party that is uncontradicted and unimpeached, at least to the extent that that evidence comes from disinterested witnesses." *Reeves*, 530 U.S. at 151, 120 S.Ct. 2097 (internal quotation marks and citation omitted).

B. Motion for a New Trial

Rule 59(a) provides, in pertinent part, "[t]he court may, on motion, grant a new trial on all or some of the issues—and to any party—as follows: . . . after a jury trial, for any reason for which a new trial has heretofore been granted in an action at law in federal court." Fed. R. Civ. P. 59(a)(1)(A). The most common reasons for granting a new trial include: (1) the verdict is against the clear weight of the evidence, and a new trial must be granted to prevent a miscarriage of justice; (2) newly discovered evidence exists that would likely alter the outcome of the trial; (3) improper conduct by an attorney or the court unfairly influenced the verdict; or (4) the verdict was facially inconsistent. See *Zarow-Smith* v. *N.J. Transit Rail Operations, Inc.*, 953 F.Supp. 581, 584-85 (D.N.J. 1997) (internal citations omitted). The decision to grant or deny a new trial is committed to the sound discretion of the district court. See *Allied Chem. Corp.* v. *Daiflon, Inc.*, 449 U.S. 33, 36, 101 S.Ct. 188, 66 L.Ed.2d 193 (1980). In the Third Circuit, "new trials because the verdict is against the weight of the evidence are proper only when the record shows that the jury's verdict resulted in a miscarriage of justice or where the verdict, on the record, cries out to be overturned or shocks [the] conscience." *Williamson* v. *Consol. Rail Corp.*, 926 F.2d 1344, 1353 (3d Cir. 1991).

Moreover, "[w]here the subject matter of the litigation is simple and within a layman's understanding, the district court is given less freedom to scrutinize the jury's verdict than in a case that deals with complex factual determinations." *Id.* at 1352 (citing *Lind* v. *Schenley Indus., Inc.*, 278 F.2d 79, 90-91 (3d Cir. 1960)); see also *Comcast Cable Commc'ns, LLC* v. *Sprint Commc'ns Co.*, 262 F.Supp.3d 118, 139 (E.D. Pa. 2017) ("Where a trial is

long and complicated and deals with a subject matter not lying within the ordinary knowledge of jurors a verdict should be scrutinized more closely by the trial judge, [in ruling on a motion for new trial], than is necessary where the litigation deals with material which is familiar and simple." (quoting *Lind*, 278 F.2d at 90-91)).

Pursuant to Rule 50(c), "[i]f the court grants a renewed motion for judgment as a matter of law, it must also conditionally rule on any motion for a new trial by determining whether a new trial should be granted if the judgment is later vacated or reversed." Fed. R. Civ. P. 50(c)(1). In addition, the court "must state the grounds for conditionally granting or denying the motion for a new trial." *Id.*

III. DISCUSSION

A. Biogen's Post-Trial Motions

Biogen moves for JMOL under Rule 50(b) as to (1) anticipation; (2) induced infringement by Pfizer; (3) induced infringement by Serono; (4) certain non-litigated defenses; and (5) certain subsidiary damages-related issues. Biogen also moves conditionally for a new trial under Rule 50(c), and alternatively for a new trial under Rule 59, on anticipation, induced infringement by Pfizer and Serono, and the subsidiary damages issues. The Court addresses each of Biogen's motions in turn with the exception of Biogen's JMOL motion as to Defendants' patent-ineligibility defense, which the Court addresses with Defendants' JMOL motion on that defense in Section III.B.1 below.

1. *Anticipation*

a. *Applicable Legal Principles for Anticipation*

A patent claim is invalid by reason of anticipation if "the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent." 35 U.S.C. § 102(a). "A prior art reference anticipates a patent's claim when the four corners of the document 'describe every element of the claimed invention, either expressly or inherently, such that a person of ordinary skill in the art could practice the invention without undue experimentation.'" *In re Hodges*, 882 F.3d 1107, 1111 (Fed. Cir. 2018) (quoting *Spansion, Inc.* v. *Int'l Trade Comm'n*, 629 F.3d 1331, 1356 (Fed. Cir. 2010)); see also *Summit 6, LLC* v. *Samsung Elecs. Co.*, 802 F.3d 1283, 1294 (Fed. Cir. 2015) ("A claim is anticipated only if each and every element is found within a single prior art reference, arranged as claimed."). The party asserting the defense bears the burden of demonstrating anticipation by clear and convincing evidence. See *Summit 6*, 802 F.3d at 1294 (citing *Microsoft Corp.* v. *i4i Ltd. P'ship*, 564 U.S. 91, 95, 131 S.Ct. 2238, 180 L.Ed.2d 131 (2011)). Anticipation is a question of fact. *In re Hodges*, 882 F.3d at 1111 (citing *Blue Calypso, LLC* v. *Groupon, Inc.*, 815 F.3d 1331, 1341 (Fed. Cir. 2016)).

Moreover, anticipation "requires the presence in a single prior art disclosure of all elements of a claimed invention arranged as in the claim. A prior art disclosure that 'almost' meets that standard may render the claim invalid under [35 U.S.C.] § 103; it does not 'anticipate.'" *Connell* v. *Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983) (internal citation omitted); see also *TF3*

Ltd. v. *Tre Milano, LLC*, 894 F.3d 1366, 1374 (Fed. Cir. 2018) ("Claims cannot be 'anticipated' by devices that are not the same. Invalidity for anticipation requires that '[t]he identical invention must be shown in as complete detail as contained in the patent claim.'" (citation omitted)); *Net MoneyIN, Inc.* v. *VeriSign, Inc.*, 545 F.3d 1359, 1371 (Fed. Cir. 2008) ("[D]ifferences between the prior art reference and a claimed invention, however slight, invoke the question of obviousness, not anticipation."); *Trintec Indus., Inc.* v. *Top-U.S.A. Corp.*, 295 F.3d 1292, 1296 (Fed. Cir. 2002) (noting that the "test for novelty" requires "strict identity"); *Jamesbury Corp.* v. *Litton Indus. Prods., Inc.*, 756 F.2d 1556, 1560 (Fed. Cir. 1985) ("[A]nticipation is not, shown by a prior art disclosure which is only 'substantially the same' as the claimed invention."), overruled on other grounds, *A.C. Aukerman Co.* v. *R.L. Chaides Constr. Co.*, 960 F.2d 1020 (Fed. Cir. 1992) (en banc); 1 Donald S. Chisum, Chisum on Patents § 3.02[1] (2018) (noting that the anticipation standard "is one of strict identity" and that "Federal Circuit decisions, explicitly or implicitly, reject any standard of 'substantial identity'" (citations omitted)).

The jury was instructed that "[f]or a claim to be invalid because it is not new" Defendants "must show by clear and convincing evidence that all of the requirements of that claim were present in a single previous device or method that was known of, used, or described in a single previous printed publication or patent." ECF No. 968 ("Final Jury Instructions") at 29. The jury instructions also provide that "[t]o anticipate the invention, the prior art does not need [to] use the same words as the claim, but all the requirements of the claim must have been disclosed, either stated expressly or implied to a person of ordinary skill in the art in the technology of the

invention, so that looking at that one reference, that person could make and use the claimed invention." *Id.*

b. *Parties' Contentions*

The jury found that the '755 patent claims were anticipated by prior-art uses of native, human interferon-β. Verdict Form at 4, Q. 12 ("Do you find, by clear and convincing evidence, that the claims of the '755 patent are invalid as anticipated by prior art uses of native human interferon-beta?"). Biogen contends that the verdict cannot stand because no reasonable jury could have found by clear and convincing evidence that the '755 patent claims were anticipated by the prior art. According to Biogen, JMOL of no anticipation under Rule 50(b) is appropriate because Defendants failed to identify a single prior-art reference that discloses all of the elements of the '755 patent claims. Biogen Br. at 13. Specifically, Biogen asserts that no reference discloses treatment with a "therapeutically effective amount" (or any amount) of a composition comprising "recombinant" interferon-β made in a "nonhuman host" that had been "transformed by a recombinant DNA molecule." *Id.* at 13-14. Instead, all therapeutic uses of interferon-β before the priority date of June 6, 1980 employed the native protein.[6] Biogen further observes that, in stark contrast to Defendants' trial presentation of their obviousness defense, Defendants did not bring a Rule 50(a) motion on anticipation at trial, "barely alluded to anticipation at trial," and did not raise anticipation in their summation. *Id.* at 5; see also 6/6/18 Tr. at 168:17-169:8. In Biogen's view, because the jury "did not focus on, and did not understand, the anticipation question," as evidenced by a jury question

[6] Defendants dispute that Biogen is entitled to a priority date of June 6, 1980, but assume that date applies for purposes of Biogen's anticipation JMOL motion. Defs. Opp. at 8 n.2.

asked only one hour before the jury returned its verdict, the verdict represents a "miscarriage of justice" warranting a new trial under Rule 59.[7] Biogen Br. at 6.

By contrast, Defendants contend that the evidence presented at trial supports the jury's verdict of anticipation. Defendants rely on the legal principle that a new source or process (i.e., recombinant DNA technology) for making an old product (i.e., interferon-β) in and of itself is insufficient to confer novelty on the product, unless the new source or process confers both structural *and* functional differences distinguishing the product from the prior art. Defs. Opp. at 1. Product claims that define a product by a particular process are referred to as "product-by-process" claims.[8] Defendants contend that this principle applies to all types of claims having source limitations, including the method of treatment claims of the

---

[7] The jury submitted a written note asking "Please explain Verdict Question #12 and its reference to 'native' human interferon beta as the basis for anticipation." ECF No. 976 at 5. In response to the jury's note, the parties agreed to provide the jury with a large-font printout of the same response that was provided to the jury during trial and which contained the parties' agreed-to definition of "native/natural interferon beta (or IFN-β)." 2/23/18 Tr. at 13:7-14:6. That definition was as follows: "Interferon beta protein that is produced naturally by human cells. Interferon beta was historically called 'fibroblast interferon' because 'fibroblasts' are one type of cell in the human body that produces interferon beta." JQX-2; JQX-2A.

[8] In support of this principle, Defendants primarily rely on a body of product-by-process case law, including *Cochrane* v. *Badische Anilin & Soda Fabrik*, 111 U.S. 293, 4 S.Ct. 455, 28 L.Ed. 433 (1884), *Purdue Pharma L.P.* v. *Epic Pharma, LLC*, 811 F.3d 1345 (Fed. Cir. 2016), *Greenliant Systems, Inc.* v. *Xicor LLC*, 692 F.3d 1261 (Fed. Cir. 2012), *Amgen Inc.* v. *F. Hoffman-La Roche Ltd.*, 580 F.3d 1340 (Fed. Cir. 2009), *SmithKline Beecham Corp.* v. *Apotex Corp.*, 439 F.3d 1312 (Fed. Cir. 2006), and *Cubist Pharmaceuticals, Inc.* v. *Hospira, Inc.*, 75 F.Supp.3d 641 (D. Del. 2014).

'755 patent. 6/6/18 Tr. at 63:7-64:2. Defendants further assert that evidence of either structural *or* functional identity between native and recombinant interferon-β can support the jury's anticipation verdict, and that there is more than sufficient evidence of both in the record. See *id.* at 65:18-66:11.

Defendants principally rely on two allegedly-anticipatory publications, Kingham *et al.*, Treatment of HBsAg-positive chronic active hepatitis with human fibroblast interferon, Gut. 19(2):91-4 (1978) ("Kingham") (STX-1596) and Sundmacher *et al.*, Human Leukocyte and Fibroblast Interferon in a Combination Therapy of Dendritic Keratitis, Albrecht Von Graefes Arch Klin Exp Ophthalmol. 208(4):229-33 (1978) ("Sundmacher") (STX-1810). Defendants contend that these publications disclose all of the elements of claim 1, specifically, the administration of therapeutically effective amounts of native, human interferon-β proteins—which, in Defendants' view, are identical to the recombinant interferon-β proteins of claim 1—to treat viral diseases. Defs. Opp. at 7-8; 6/6/18 Tr. at 61:6-18.

In addition, Defendants rely on two comparative studies that, while not prior art, allegedly demonstrate that the native interferon-β administered in Kingham and Sundmacher is structurally identical to interferon-β made recombinantly in Chinese Hamster Ovary ("CHO") cells: a study by InterPharm Laboratories Ltd. entitled "Comparative Biochemical Analysis of Native Human Fibroblast Interferon and Recombinant Beta Interferon Expressed by Chinese Hamster Ovary Cells" (the "InterPharm Study") (STX-1259),[9] and Kagawa *et al.*, Com-

[9] The InterPharm Study was prepared no earlier than 1987. See STX-1259 (InterPharm Study) at 1, 14; 2/9/18 Tr. at 89:6-18 (Lodish).

parative Study of the Asparagine-linked Sugar Chains of Natural Human Interferon-β1 and Recombinant Human Interferon-β1 Produced by Three Different Mammalian Cells, J Biol Chem. 263(33): 17508-15 (1988) ("Kagawa") (STX1587). In support of their position that native and recombinant interferon-β are functionally identical, Defendants rely on the InterPharm Study, along with a publication co-authored by Michel Revel, M.D., Ph.D., Professor Emeritus retired from the Weizmann Institute of Science, entitled Chernajovsky *et al.*, Efficient Constitutive Production of Human Fibroblast Interferon by Hamster Cells Transformed with the IFN-β1 Gene Fused to An SV40 Early Promoter, DNA 3(4):297-308 (1984) ("Chernajovsky") (STX-1439), and Dr. Revel's United States Patent No. 4,808,523 (the "Revel '523 patent") (STX-1314). Defs. Opp. at 13. As with the InterPharm Study and Kagawa, neither Chernajovsky nor the Revel '523 patent is prior art.

Finally, Defendants rely on the expert testimony of Harvey Lodish, Ph.D., a Professor of Biology and Biological Engineering at the Massachusetts Institute of Technology and member of the Whitehead Institute for Biomedical Research. 2/8/18 PM Tr. at 48:21-49:1. Defendants offered Dr. Lodish as an expert in the field of recombinant DNA technology and the production of recombinant therapeutic proteins. *Id.* at 57:9-16. In Defendants' view, JMOL is inappropriate because there was sufficient evidence in the record for the jury to conclude that native interferon-β administered before June 6, 1980 and recombinant interferon-β made in CHO cells are structurally identical, functionally identical, or both.

c. *Biogen Is Entitled to JMOL of No Anticipation*

In assessing the sufficiency of the evidence, the Court gives Defendants, as the verdict winners, "the benefit of all logical inferences that could be drawn from the evidence presented, resolve[s] all conflicts in the evidence in [Defendants'] favor and, in general, view[s] the record in the light most favorable to [Defendants]." *Williamson*, 926 F.2d at 1348. After reviewing the evidence presented at trial, the Court concludes that there is insufficient evidence to support the jury's verdict that the prior-art uses of native, human interferon-β anticipate the '755 patent claims.

i) Defendants Failed to Present as Evidence a Prior-Art Reference Disclosing Each and Every Element of the '755 Patent Claims

The Court concludes that because Defendants failed to present as evidence a single prior-art reference that describes the therapeutic use of a recombinant interferon-β polypeptide made in a non-human host, the jury could not have reasonably reached its verdict of anticipation. As discussed above, the '755 patent claims are method claims that require therapeutic use of a recombinant interferon-β polypeptide made in a non-human host. The Court instructed the jury that a "recombinant polypeptide" is "a polypeptide produced by recombinant DNA engineering," that a "recombinant DNA molecule" must include "DNA from different genomes," and that "produced in a nonhuman host transformed by a recombinant DNA molecule" requires production within "a transformed cell line that is not a human cell line." Final Jury Instructions at 17. Defendants failed to identify a single prior-art reference that discloses all of the elements of

the '755 patent claims. Specifically, no reference in the record discloses treatment with a "therapeutically effective amount" of a composition comprising a "recombinant" interferon-β polypeptide produced in a "non-human host" that had been "transformed by a recombinant DNA molecule."

Instead, the expert testimony presented to the jury, including testimony by Defendants' experts Dr. Lodish and Jordan Gutterman, M.D., the latter a Professor of Medicine at the University of Texas MD Anderson Cancer Center, showed that all therapeutic uses of interferon-β before the priority date of June 6, 1980 employed native, human interferon-β.[10] See 2/13/18 AM Tr. at 35:4-37:5 (Lodish) (explaining that before June 6, 1980, no one had made enough recombinant interferon-β to treat a patient); 2/7/18 PM Tr. at 85:7-86:7 (Gutterman) (explaining that studies of interferon-β in MS in the 1970s did not use "recombinant interferon" but instead used "the native interferon produced from fibroblasts"); 2/15/18 PM Tr. at 66:12-16 (Garcia) (agreeing that no prior-art publications "talked about the activity of recombinant beta interferon"). The '755 patent itself discloses that therapeutic use of native, human interferon-β was known in the prior art, and describes how compositions of the native protein had been prepared. PTX0001 ('755 patent) at 2:53-4:22, 4:49-5:3. Although Defendants cite prior-art publications disclosing therapeutic uses of interferon-β, those uses were

---

[10] Additional testimony in the record showed that before June 6, 1980, native, human interferon-β was used and studied for the treatment of viruses, cancers, and other diseases, including MS. See, *e.g.*, 1/29/18 PM Tr. at 83:9-15 (Rudick); 2/7/18 AM Tr. at 43:9-44:13, 45:9-11, 91:21-92:11 (Gutterman); 2/7/18 PM Tr. at 46:20-47:2 (Gutterman); 2/9/18 Tr. at 77:16-79:7 (Lodish); 2/14/18 AM Tr. at 12:17-13:7 (Revel).

limited to the native protein. See STX-1596 (Kingham) at 1 (disclosing use of native, human interferon-β for the treatment of hepatitis B virus); STX-1810 (Sundmacher) at 1 (disclosing use of native, human interferon-β for the treatment of dendritic keratitis virus). Defendants did not present any evidence or testimony as to the presence in the prior art of therapeutic uses of recombinant interferon-β.

Accordingly, since Defendants failed to present as evidence a single prior-art reference that discloses each and every element of the '755 patent claims, no reasonable jury could have found by clear and convincing evidence that the claims were anticipated by the prior art. See *Summit 6*, 802 F.3d at 1294 ("A claim is anticipated only if each and every element is found within a single prior art reference, arranged as claimed.").

ii) JMOL of No Anticipation Is Appropriate Even Applying Product-By-Process Law

Even if the Court were to agree with Defendants that method of treatment claims having source limitations should be analyzed in the same way as product-by-process claims for purposes of anticipation, or that the Court should at least be guided by product-by-process law, the jury's verdict of anticipation still cannot stand. Giving Defendants the benefit of every fair and reasonable inference that can be drawn from the record, as discussed below, there is insufficient evidence to support a finding that the product of the '755 patent claims (i.e., recombinant interferon-β made, for example, in CHO cells) is the same as the product known and used in the prior art (i.e., native interferon-β).

1) Native and Recombinant Interferon-β Are Not Structurally Identical

The evidence presented at trial demonstrates that native interferon-β and recombinant interferon-β are not structurally identical. As discussed above, "strict identity" is a requirement for anticipation; that the prior art is "substantially identical," "extremely similar," or "very similar" to the claimed invention is not enough. See *Trintec*, 295 F.3d at 1296 (noting that the "test for novelty" requires "strict identity"); *Jamesbury*, 756 F.2d at 1560 ("[A]nticipation is not shown by a prior art disclosure which is only 'substantially the same' as the claimed invention."); *Connell*, 722 F.2d at 1548 (rejecting argument that "it is sufficient for an anticipation if the general aspects are the same and the differences in minor matters is only such as would suggest itself to one of ordinary skill in the art" as "[t]hose statements relate to obviousness, not anticipation" (internal quotation marks omitted)).

Although Defendants contend that the "most basic and obvious identicality between [native and recombinant interferon-β] proteins is in the DNA," (6/6/18 Tr. at 74:23-24), and that the "amino acid sequence of both proteins is identical," (*id.* at 75:20-21), the record evidence shows that the proteins differ structurally in terms of their attached carbohydrate (or sugar) groups, also referred to as glycosylation patterns. In denying Bayer's Motion for Summary Judgment of Invalidity No. 2 (Anticipation by the Treatment References), which Defendants joined, the Court declined to find as a matter of law that "their shared amino acid sequence renders native interferon-β and recombinant interferon-β the same for purposes of anticipation." ECF No. 892 ("Summ. J. Op.") at 28. In

reading the term "polypeptide" in the context of claim 1, the Court determined that claim 1 requires the recombinant polypeptide to display "antiviral activity" and be administered in a "therapeutically effective amount." *Id.* The Court concluded that "for a polypeptide to display biological activity, it must be folded into its appropriate three-dimensional structure." *Id.* That the native and recombinant interferon-β proteins share the same linear amino acid sequence is not enough for purposes of anticipation. Rather, the appropriate analysis is to compare the three-dimensional structure of the prior-art native interferon-β with the recombinant interferon-β of claim 1, which include the structures of any attached carbohydrate groups.

Moreover, Defendants' expert, Dr. Lodish, testified during his direct examination that the native and recombinant proteins' structures are *not* identical with respect to their carbohydrate groups. Among the several opinions Dr. Lodish discussed during the three days on which he testified as the brief statement that, in his view, native interferon-β and recombinant interferon-β are, at best, "substantially identical." 2/8/18 PM Tr. at 50:11-12. Specifically, during a short portion of one afternoon session at trial, he testified that, based on his reading of the InterPharm Study, "[t]here were minor differences in the structures of the sugars" of native and recombinant interferon-β, "but I wouldn't call them identical, I would call the sugars extremely similar."[11] 2/9/18 Tr. at 87:24-

[11] Defendants point to the ultimate conclusion of the InterPharm Study: "Based on the above sections, it can be concluded that recombinant beta interferon derived from CHO cells (RBIF) is identical to human fibroblast interferon (HFIF)." STX-1259 (InterPharm Study) at 122. Although the Court draws reasonable inferences in Defendants' favor, contrary to Defendants' assertion, the statement under the "Conclusion" heading at the very end of the InterPharm

88:7; see also *id.* at 87:3-9 (explaining that although he did not perform a comparison of native interferon-β in the prior art with recombinant interferon-β made in CHO cells, he would characterize the amino acid sequences as "exactly" the same but the carbohydrates as "virtually identical"); STX-1259 (InterPharm Study) at 94 (concluding that the sugar structures of native and recombinant interferon-β are merely "very similar"). Additional expert testimony in the record offered a consistent interpretation of the InterPharm Study. See 2/15/18 PM Tr. at 101:9-102:15 (Garcia) (stating that with respect to the glycosylation patterns of the native and recombinant proteins, "[i]n some cases they're close, but they're never identical," and that it is "pretty clear that the[ ] glycans have some significant differences"). Dr. Lodish also testified that Kagawa showed that the sugar groups of the native and recombinant proteins in the study had "small differences" that made them "extremely similar." 2/9/18 Tr. at 88:9-25. These "minor" and "small" differences

---

Study falls short of constituting clear and convincing evidence, particularly upon review of the document as a whole and its more detailed statements and analyses underlying this conclusory statement. In particular, the InterPharm Study reveals that the molecules in the recombinant interferon-β material are structurally different from the molecules of the native material. See *id.* at 94 (concluding that the glycosylation patterns are merely "very similar"); 6/6/18 Tr. at 27:18-29:21. Indeed, Defendants elicited testimony by Dr. Lodish where he disagreed with the InterPharm Study's ultimate conclusion on page 122 of the document that the native and recombinant proteins are "identical," stating that he "wouldn't call them identical." 2/9/18 Tr. at 87:24-88:7. On JMOL, the Court should not rely on conclusory statements that purport to controvert specific statements in the record. See *Koito Mfg. Co.* v. *Turn-Key-Tech, LLC*, 381 F.3d 1142, 1152 (Fed. Cir. 2004). A reasonable jury would not rely solely on that single statement under the "Conclusion" heading in the InterPharm Study and ignore contrary expert testimony and the detailed analyses throughout the document.

matter for purposes of anticipation. See *Net MoneyIN*, 545 F.3d at 1371 ("[D]ifferences between the prior art reference and a claimed invention, *however slight*, invoke the question of obviousness, not anticipation." (emphasis added)).

In their opposition brief, Defendants explain that Dr. Lodish's testimony was "*not* that the individual polypeptides differed, but instead that the *proportions* of polypeptides containing *identical* sugar structures in IFN-β made naturally and recombinantly were 'extremely similar.'" Defs. Opp. at 14 (quoting 2/9/18 Tr. at 87:14-88:25, 103:6-10 (Lodish)) (emphasis in original). Defendants assert that the "prior art mixtures" of native interferon-β proteins encompass species of proteins that are identical to species of recombinant interferon-β proteins covered by the '755 patent claims. See *id.* Defendants rely on Kagawa's purported teaching that "IFN-β made naturally is actually a mixture of proteins having distinct structures, and the same is true of IFN-β made in CHO cells with recombinant DNA technology," and that two such distinct structures (Structures I and V) disclosed in Kagawa are "common to both native and CHO IFN-β." *Id.* at 12-13 (citing STX-1587 (Kagawa) at 4 (Table III)). In Defendants' view, Kagawa shows that the "overwhelming majority of IFN-β made in CHO cells (95%) is structurally *identical* to specific protein molecules found in IFN-β made naturally," and the prior-art treatments disclosed in Kingham and Sundmacher "therefore *necessarily included* the administration of specific IFN-β polypeptides (Structures I and V) that are *structurally identical* to IFN-β polypeptides made in CHO cells and within the scope of the '755 patent claims." *Id.* at 13 (emphasis in original). Defendants contend that Biogen improperly focuses on Dr. Lodish's testimony regarding structural

differences between the "mixtures" or "populations" of native and recombinant proteins as groups, and that the "pertinent question is whether the prior art disclosed the administration of a composition including any polypeptide with the same structure as any polypeptide whose use that '755 patent claims cover." *Id.* at 14. In other words, in Defendants' view, it is sufficient for anticipation purposes if within a population of native interferon-β proteins there are some molecules that are the same as (i.e., atomically identical to) some molecules within a population of recombinant interferon-β proteins even if the populations themselves are not identical.[12] See 6/6/18 Tr. at 116:10-117:11, 138:2-22.

---

[12] In their brief, Defendants cite the principle that a prior-art species can anticipate a claimed genus that encompasses that species. See Defs. Opp. at 14. The Court is not persuaded that the law Defendants cite applies in this case. In addition, the district court in *Amgen* rejected a similar argument. As discussed below, *Amgen* involved patents related to the production of recombinant protein erythropoietin ("EPO"). The defendant, Roche, argued that the source limitation of the claim at issue (the claimed recombinant EPO is "purified from mammalian cells grown in culture") did not distinguish recombinant EPO over the prior-art urinary EPO. *Amgen, Inc.* v. *F. Hoffman-La Roche Ltd.*, 581 F.Supp.2d 160, 197 (D. Mass. 2008), aff'd in part, vacated in part, remanded sub nom. *Amgen Inc.*, 580 F.3d 1340. Specifically, Roche argued that the source limitation was "so vague that it embraces a myriad of hypothetical EPO structures that might be 'structurally indistinguishable . . . from human urinary EPO'" and therefore "any distinctions between human and urinary EPO that are caused by differences in purification techniques cannot establish novelty." *Id.* (citation omitted). The court reiterated that Roche had the burden of proving that urinary EPO "was in fact identical to the EPO described in" the claim, and concluded that the "mere fact that some mammalian cell purified in some manner in some culture *might* produce some glycoprotein structurally similar to [urinary] EPO hardly roves anticipation by clear and convincing evidence." *Id.* (emphasis in original); see also *Amgen*, 580 F.3d at 1364 (noting that the district court "rejected Roche's contention that

Even if the Court were to accept Defendants' anticipation theory, the anticipation evidence remains critically deficient. Defendants have not cited any testimony, from Dr. Lodish or otherwise, stating that as between two populations—native interferon-β proteins in the prior art and recombinant interferon-β proteins—there is a molecule or subset of molecules that is identical between them. See *id.* at 120:7-23, 123:7-22, 130:9-132:23, 133:7-136:13, 139:4-140:24, 143:25-145:16. The few lines of trial testimony from Dr. Lodish upon which Defendants rely neither expressly nor implicitly elucidate this theory for the jury. Based on a review of the record, it does not appear that the particular arguments that Defendants have raised post-trial to uphold the anticipation verdict were, in fact, presented to the jury either through expert testimony, during summation, or otherwise. Although Defendants assert that "the InterPharm report and the Kingham or Sundmacher papers TTT would be sufficient in and of itself to support this jury verdict," (*id.* at 77:3-8), neither Dr. Lodish nor any other witness at trial testified as to the presence in the prior art of the particular protein structures identified in the InterPharm Study or any of the other post-June 6, 1980 references. In other words, there was no evidence presented to the jury "linking" the prior-art use of native, human interferon-β as disclosed in Kingham, Sundmacher, or any other prior-art reference with the InterPharm Study, Kagawa, Chernajovsky, or the Revel '523 patent. See *id.* at 22:12-23:3. Without any evidence or testimony in the record

---

. . . urinary EPO anticipated [the claim at issue] because at least some of the recombinant EPO would be structurally indistinguishable from urinary EPO"). In other words, even if there may be some molecules that are identical between non-identical populations, that fact alone does not suffice to anticipate.

mentioning, let alone explaining, that there is a molecule that exists in both the prior-art native interferon-β population and the recombinant interferon-β population, it cannot fairly be concluded that the jury drew such an inference in reaching its verdict.

The evidence Defendants cite in support of their anticipation theory is deficient in other respects as well. For instance, there appears to be no evidence or testimony that the native interferon-β proteins used in the prior art are the same as the native proteins studied in the post-June 6, 1980 publications. Absent from the record is any evidence of the carbohydrate structure of a single native interferon-β protein used for treatment in the prior art. Sundmacher does not disclose the structure of the native interferon-β material, including its glycosylation pattern, nor is it clear what cell lines were used in the study. Kingham similarly does not disclose the glycosylation pattern of the native interferon-β produced from the human fetal lung fibroblast cells used in the study. Moreover, there was no testimony from any witness regarding the structures of the native proteins discussed in either of those prior-art publications. Also absent from the record is any testimony that all native, human interferon-β proteins are structurally identical. Indeed, the InterPharm Study and Kagawa disclose different compositions for native, human interferon-β proteins. See 6/6/18 Tr. at 104:14-106:9; STX-1587 (Kagawa) at 4; STX-159 (InterPharm Study) at 67 (stating that "[a]n analysis of oligosaccharide [or carbohydrate] structures on the same protein from different species and even different tissues reveals that major variations frequently exist" and that "a homogeneous cell population" produces "an astonishing array of different oligosaccharide structures"). Furthermore, the InterPharm Study offers almost no infor-

mation about the precise native, human interferon-β proteins used in the study, whether those proteins pre-dated the priority date, or whether the study used the same cell line or cell type as that used in either Kingham or Sundmacher.

In sum, Defendants bore the burden of proving by clear and convincing evidence that the native, human interferon-β in the prior art was in fact identical to the recombinant interferon-β of the '755 patent claims. Given the above-mentioned deficiencies in the evidence, no reasonable jury could find that Defendants met their burden.

2) Native and Recombinant Interferon-β Are Not Functionally Identical

The evidence presented at trial also demonstrates that native, human interferon-β and recombinant interferon-β are not functionally identical. Although Dr. Lodish testified that the functional characteristics of native interferon-β and recombinant interferon-β made in CHO cells are "very similar, if not identical," (2/9/18 Tr. at 87:10-13), as discussed above, "strict identity" is required for anticipation. Defendants rely on the InterPharm Study, Chernajovsky, and the Revel '523 patent as evidence of functional identity. See Defs. Opp. at 13; STX-1439 (Chernajovsky) at 2 (stating that recombinant interferon-β "appears identical in size, activity, and immunospecificity to the native human IFN-β1 glycoprotein"); STX-1314 (Revel '523 patent) at 10 (stating that "expression of the DNA coding for pre-IFN-β1 in hamster cells leads to the secretion of a protein which is electrophoretically identical to the natural glycoprotein and which gives, upon purification by immunoaffinity on monoclonal antibodies, the same specific activity as the IFN-β1 purified from human fibroblasts"). As discussed above, however, there

was no evidence presented to the jury "linking" the prior-art use of native, human interferon-β disclosed in Kingham and Sundmacher with the InterPharm Study, Chernajovsky, or the Revel '523 patent.

Moreover, the jury heard fact and expert testimony regarding the different biological effects that native interferon-β and recombinant interferon-β have on the human body. Biogen's expert, Revere Kinkel, M.D., a neurologist at the University of California San Diego, testified regarding the role of neutralizing antibodies in interferon-β treatment. 1/29/18 PM Tr. at 12:16-15:18. Dr. Kinkel explained that neutralizing antibodies are proteins that bind to interferon and prevent it from binding to its receptor and having its intended effect. *Id.* at 14:3-8. Dr. Kinkel opined that the closer a recombinant protein resembles the native protein, the lower the development of neutralizing antibodies. *Id.* at 13:1-10. Dr. Kinkel also testified about the differences among the various recombinant interferon-β drug products Betaseron®, Extavia®, Rebif®, Avonex®, and Plegridy® in terms of the incidence of neutralizing antibodies. *Id.* at 14:9-15:18.

The evidence presented at trial also showed that recombinant interferon-β can be made in much larger quantities and much more easily than native, human interferon-β can be obtained. See, *e.g.*, PTX0001 ('755 patent) at 4:10-13, 4:49-61, 6:64-67. In particular, the '755 patent explains that interferon-β "produced by human cell lines grown in tissue culture" resulted in a "low yield, expensive process." *Id.* at 4:49-50; see also *id.* at 4:11-13 (noting that "the antitumor and anticancer applications of IFN-β have been severely hampered by lack of an adequate supply of purified IFN-β"). This problem was eventually solved by

> locating and separating DNA sequences that code for the expression of HuIFN-β in an appropriate host thereby providing DNA sequences, recombinant DNA molecule and methods by means of which a host is transferred to produce a polypeptide displaying an immunological or biological activity of human fibroblast interferon.

Id. at 6:48-53. By virtue of this discovery, it was "possible to obtain polypeptides displaying an immunological or biological activity of HuIFN-β for use in antiviral, antitumor or anticancer agents and methods," and the invention "allow[ed] the production of these polypeptides in amounts and by methods" that were not previously available "for use in antiviral and antitumor or anticancer agents and methods and immunomodulation." *Id.* at 6:54-7:7; see also *Amgen Inc.* v. *F. Hoffman-La Roche Ltd.*, 580 F.3d 1340, 1364 (Fed. Cir. 2009) (referring to functional differences between the prior-art native protein and claimed recombinant protein that formed the basis of the district court's finding of no anticipation, including the recombinant protein's "ability to be mass produced"). Defendants did not offer contrary evidence with respect to these particular functional differences. See *Reeves*, 530 U.S. at 151, 120 S.Ct. 2097 (explaining that while the district court "must disregard all evidence favorable to the moving party that the jury is not required to believe" it should "give credence" to the "evidence supporting the moving party that is uncontradicted and unimpeached").

Furthermore, although the evidence establishes functional differences, it appears that structural differences alone may suffice to impart novelty. This case is similar to *Amgen, Inc.* v. *F. Hoffman-La Roche Ltd.*, 581 F.Supp.2d 160 (D. Mass. 2008), which involved patents

related to the production of a protein called erythropoietin, also known as EPO, using recombinant DNA technology. The claims at issue covered EPO and pharmaceutical compositions thereof and included source limitations—i.e., the EPO was "purified from mammalian cells grown in culture" or was the "product of . . . expression in a mammalian host cell." *Id.* at 193, 206. The district court concluded, and the Federal Circuit affirmed, that the claims to recombinant EPO were not anticipated by the prior-art native EPO that had been isolated from human urine based on differences in carbohydrate structures between the recombinant protein and the native protein.[13] *Id.* at 195; *Amgen*, 580 F.3d at 1367-69. Those "structural distinctions," which were "attributable to recombinant EPO's source," meant that "no reasonable jury could find that the recombinant EPO described in the asserted claims . . . was an old product." *Amgen*, 580 F.3d at 1368-69.

Notably, the Federal Circuit made no mention of functional differences in affirming the anticipation rulings. After analyzing and finding sufficient bases to uphold those rulings, the Federal Circuit then addressed the defendant Roche's challenge to the district court's decision to construe the source limitations differently in the validity and infringement contexts. *Id.* at 1369-70. In so doing, the Federal Circuit noted that the district court had found, based on the record in the case, that "urinary EPO

---

[13] The defendant Roche brought an anticipation challenge against two patents. With respect to the first patent, the district court granted the plaintiff's Rule 50(a) JMOL motion of no anticipation rather than submit the issue to the jury. *Amgen*, 580 F.3d at 1364. The issue of anticipation as to the second patent was sent to the jury, and the district court sustained the jury's verdict of no anticipation. *Id.* The Federal Circuit upheld both anticipation rulings. *Id.* at 1367-69.

and recombinant EPO were structurally and functionally different." *Id.* at 1370. Although Defendants focus on this language from the decision, the holding of novelty in Amgen was based on structural differences, and at no point in its decision did the Federal Circuit state that functional differences were required.[14] See *United Therapeutics Corp.* v. *Sandoz, Inc.*, Nos. 12-1617, 13-316, 2014 WL 4259153, at *52 (D.N.J. Aug. 29, 2014) ("Structural differences alone may distinguish the prior art." (citing *Greenliant Sys., Inc.* v. *Xicor LLC*, 692 F.3d 1261, 1269-

[14] Defendants also cite *Purdue*, *Greenliant*, and *Cubist* to support their position that both structural *and* functional differences are required to defeat anticipation. These cases merely reiterate the principle announced in *Amgen* that structural and functional differences are "relevant as evidence of no anticipation" and decide validity based on the particular facts of each case; they do not impose a requirement to show both structural and functional differences. *Greenliant* quotes the language from *Amgen*, but also cites the Manual of Patent Examining Procedure in stating that, consistent with Federal Circuit precedent, the United States Patent and Trademark Office ("PTO") "in determining patentability considers the process in which a product is formed if that process imparts distinctive *structural* characteristics." 692 F.3d at 1268 (emphasis added). In that case, the applicant told the PTO that its claimed invention had distinct structural characteristics as compared to the prior art, which the Federal Circuit relied on in determining whether the claims at issue were invalid under the rule against recapture. See *id.* at 1269-72. The Federal Circuit in *Purdue* concluded that since the source limitation at issue "impart[ed] no structural *or* functional differences," the district court "did not err in disregarding the process limitation in its obviousness determination." 811 F.3d at 1354 (emphasis added). Finally, in *Cubist*, the patentee argued that the claimed "composition free from [two impurities] [was] structurally and functionally different from the prior art composition." 75 F.Supp.3d at 668-69. In other words, in Cubist it was argued that the low level of impurity of the claimed invention was both a structural *and* a functional difference, and the district court found there was no difference, either structurally *or* functionally. *Id.* at 669.

71 (Fed. Cir. 2012))); Manual of Patent Examining Procedure §2113 (9th ed. Rev. Aug. 2017) ("The *structure* implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart *distinctive structural characteristics* to the final product." (emphasis added)); 3 Donald S. Chisum, Chisum on Patents §8.05[3] (2018) ("Even though a product may be claimed in terms of the process of making it, the product still must be new in *structural* terms in order to meet the novelty requirement." (emphasis added) (citing *Cochrane* v. *Badische Anilin & Soda Fabrik*, 111 U.S. 293, 4 S.Ct. 455, 28 L.Ed. 433 (1884); *SmithKline Beecham Corp.* v. *Apotex Corp.*, 439 F.3d 1312 (Fed. Cir. 2006))).[15]

iii) Product-By-Process Law Should Not Apply in Analyzing the Validity of the '755 Patent Method of Treatment Claims

---

[15] Defendants argue that in *Amgen*, unlike in this case, the structural differences in terms of carbohydrate compositions between native and recombinant EPO led to functional differences in terms of specific activity and stability in the human body. 6/6/18 Tr. at 69:2-70:11, 156:8-16. Biogen disagrees with Defendants' assertion that the evidence in this case shows that glycosylation of interferon-β is unimportant. *Id.* at 158:1-17. According to Biogen, the evidence shows that structural differences in terms of glycosylation patterns lead to functional differences in terms of efficacy. See *id.* As discussed above, the record evidence reveals structural and functional differences between native and recombinant interferon-β. Moreover, *Amgen* does not appear to require that structural differences result in functional differences.

The Court has addressed the issues raised in Biogen's JMOL motion under the framework proposed by Biogen. The Court has also addressed those issues under the framework proposed by Defendants. Under either approach, the Court has concluded that there is legally insufficient evidence to support the jury's verdict of anticipation. Nevertheless, for the following reasons, the Court concludes that Biogen's proposed framework is more appropriate in this case.

As an initial matter, there appears to be no binding precedent supporting Defendants' position that the anticipation inquiry of product-by-process claims governs the analysis of method of treatment claims that include source limitations, such as claim 1 of the '755 patent. The parties agree that claim 1 includes a source limitation, i.e., the interferon-β protein is made by recombinant DNA technology. In its claim construction Opinion, this Court stated that it was "unclear that [the] method of treatment claim can be treated as a product-by-process claim," and that it was "aware of no binding precedent requiring method of treatment claims to be treated as product-by-process claims in the claim construction context." *Markman* Op. at 14. Since the Court's claim construction ruling, Defendants have not identified cases that would warrant this Court to apply the framework for assessing novelty of product-by-process claims to method of treatment claims.[16]

---

[16] Defendants cite *Leggett* v. *Standard Oil Co.*, 149 U.S. 287, 13 S.Ct. 902, 37 L.Ed. 737 (1893) as an example where product-by-process law was purportedly applied to method claims. The Court is not persuaded that Leggett compels the application of product-by-process law in the determination of validity of method claims. Indeed, the Court agrees with Biogen's reading of *Leggett* as a straightforward anticipation case, which Defendants ask this Court to apply in a way

Even beyond the absence of binding precedent, the Court is persuaded by Biogen's argument that given the particular principles underlying product-by-process law, the framework Defendants propose *should not* apply to assessing the validity of the '755 patent method of treatment claims.[17] The product-by-process doctrine allows patentees to draft claims to a product by reference to the process by which the product is made where the product's characteristics are unknown or otherwise cannot be described. See *In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985). As the Federal Circuit explained:

> Product-by-process claims are not specifically discussed in the patent statute. The practice and governing law have developed in response to the need to enable an applicant to claim an otherwise patentable product that resists definition by other than the process by which it is made. For this reason, even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself.

---

that no court appears to have previously done. Specifically, the claims in *Leggett* were directed to a process of coating or lining the inside of barrels with unsolidified glue to make the barrels waterproof. *Id.* at 288-89, 13 S.Ct. 902. The Supreme Court concluded that the claims were anticipated, noting that the process of lining barrels with glue that had not previously been solidified had been practiced in the prior art. *Id.* at 295-97, 13 S.Ct. 902 (noting that others in the industry were using liquid glue that had never been dried in the same manner as claimed). In other words, the identical process had been practiced in the prior art.

[17] Moreover, as discussed below with respect to the issue of patent eligibility under 35 U.S.C. § 101, fundamental policy differences inform how the law treats method of treatment claims as opposed to product claims, at least in the context of patent eligibility.

Id. (citations omitted). The purpose of the doctrine is to prevent foreclosing inventors "from the benefits of the patent system simply because a product is difficult to describe in words, or its structure is insufficiently understood." *SmithKline*, 439 F.3d at 1315. For purposes of infringement, the product-by-process claim will only cover products that are made by the claimed process, whereas for purposes of validity, the "focus is on the product and not on the process of making it." *Amgen*, 580 F.3d at 1369-70 (citations omitted); see also *id.* at 1370 ("[A] product in the prior art made by a different process can anticipate a product-by-process claim, but an accused product made by a different process cannot infringe a product-by-process claim.").

Claim 1 of the '755 patent, by contrast, is not directed to a product that the inventor, Dr. Walter Charles Fiers, was unable to describe in words or where the product's structure was not sufficiently understood. Rather, the purpose of the invention, consistent with the stated goal of the '755 patent, was to solve the problem in the prior art that the viability of certain medical treatments was hindered by insufficient supply. See PTX0001 ('755 patent) at 4:10-13; 6:54-7:7. The principles that inform product-by-process law as set forth in *Thorpe*, *SmithKline*, and *Amgen* do not apply in this context. See 6/6/18 Tr. at 12:10-11 (explaining that the '755 patent "is not taking advantage of a legal procedure to overcome a lack of information"). The Court agrees with Biogen that since the source limitation of claim 1 "lies at the heart of the benefit of this invention," it should be given "force and effect in the anticipation analysis." *Id.* at 12:7-10.

The procedural posture dictates that the Court may only consider whether Defendants presented sufficient evidence to support the jury's conclusion. Even viewing

the evidence in the light most favorable to Defendants, the Court concludes that there is insufficient evidence from which the jury reasonably could have found that the '755 patent claims were anticipated by the prior-art uses of native, human interferon-β. Accordingly, the Court grants Biogen's Rule 50(b) JMOL motion of no anticipation and vacates the jury's verdict in favor of Defendants.

d. *Biogen Is Entitled to a Conditional New Trial on Anticipation*

For the same reasons the Court grants Biogen's JMOL motion, the Court conditionally orders a new trial on anticipation pursuant to Rule 50(c)(1). Additional considerations warrant granting Biogen's request for a new trial on the issue of anticipation. The Court recognizes that the five-week trial in this case was "long and complicated," required complex factual determinations on multiple infringement, validity, and damages issues, was noticeably focused on issues other than anticipation, and involved scientific concepts that are not the "subject matter . . . lying within the ordinary knowledge of jurors." *Lind*, 278 F.2d at 90-91. Thus, the jury verdict deserves close scrutiny. See *Comcast*, 262 F.Supp.3d at 139 (applying "close scrutiny" to the verdict and conditionally granting a new trial under Rule 50(c)(1) following a 14-day patent trial involving "the complexities of cellular networks"). The jury spent the vast majority of the trial hearing fact and expert testimony on issues other than anticipation; indeed, in contrast with their other invalidity theories, Defendants did not mention anticipation or Question 12 of the Verdict Form once in their summation. Moreover, although a jury is free to draw reasonable inferences from the evidence presented, here the verdict of anticipation appears to rest on a number of inferences

that Defendants did not argue to the jury. See *Roebuck* v. *Drexel Univ.*, 852 F.2d 715, 735-36 (3d Cir. 1988).

Upon consideration of the overall setting of the trial, the character of the evidence, and the complexity of the legal principles that the jury was asked to apply to the facts, the Court concludes that the jury's determination that the '755 patent claims are invalid for anticipation is against the weight of the evidence and therefore warrants the conditional grant of a new trial on the issue of anticipation pursuant to Rule 50(c)(1). Biogen's alternative request for a new trial under Rule 59 is denied as moot.

2. *Induced Infringement By Pfizer and Serono*

Biogen seeks JMOL of induced infringement against Pfizer and Serono. As to the questions of direct infringement by healthcare professionals and/or patients and contributory infringement by Pfizer and Serono, the jury found in favor of Biogen. Defendants have not challenged the jury's finding of direct infringement or its finding of contributory infringement by Serono. Nevertheless, because the legal principles for, and specific elements of, each type of infringement are instructive to the following analysis regarding the issue of induced infringement, the Court discusses those principles and elements below.

a. *Applicable Legal Principles for Direct, Induced, and Contributory Infringement*

Section 271(a) of the Patent Act governs direct infringement and provides that "whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States . . . during the term of the patent therefor, infringes the patent." 35 U.S.C. § 271(a). Section 271(b) of the Patent Act governs induced infringement and provides that "[w]hoever actively induces

infringement of a patent shall be liable as an infringer." 35 U.S.C. §271(b). In order to prevail on an inducement claim, the patentee must establish "first that there has been direct infringement, and second that the alleged infringer knowingly induced infringement and possessed specific intent to encourage another's infringement." *ACCO Brands, Inc.* v. *ABA Locks Mfrs. Co.*, 501 F.3d 1307, 1312 (Fed. Cir. 2007) (quoting *Minn. Mining & Mfg. Co.* v. *Chemque, Inc.*, 303 F.3d 1294, 1304-05 (Fed. Cir. 2002)). "'To prove inducement of infringement, the patentee must [ ]show that the accused inducer took an affirmative act to encourage infringement with the knowledge that the induced acts constitute patent infringement." *Power Integrations*, 843 F.3d at 1332 (quoting *Astornet Techs. Inc.* v. *BAE Sys., Inc.*, 802 F.3d 1271, 1279 (Fed. Cir. 2015)).

In addition, a reasonable, good-faith belief in noninfringement can negate the specific intent required for induced infringement. See *Commil USA, LLC* v. *Cisco Sys., Inc.*, 720 F.3d 1361, 1367-68 (Fed. Cir. 2013) ("[I]t is clear that a good-faith belief of non-infringement is relevant evidence that tends to show that an accused inducer lacked the intent required to be held liable for induced infringement." (citations omitted)), vacated and remanded on other grounds, —— U.S. ——, 135 S.Ct. 1920, 191 L.Ed.2d 883 (2015). This defense applies where such a belief is based on a reasonable reading of the patent claims, even if that reading is later found to be incorrect.[18] See *Commil*, 135 S.Ct. at 1928.

---

[18] During trial, the Court ruled that although a good-faith belief in a rejected claim construction can be asserted as a defense to negate the specific intent required to induce infringement, such a belief is not a defense to negate the lesser knowledge requirement of contributory infringement. 2/20/18 PM Tr. At 10:1-8.

Section 271(c) of the Patent Act governs contributory infringement and provides that:

> [w]hoever offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial noninfringing use, shall be liable as a contributory infringer.

35 U.S.C. § 271(c). Unlike induced infringement, contributory infringement under § 271(c) requires "only proof of a defendant's *knowledge*, not *intent*, that his activity cause infringement." *Lifetime Indus., Inc.* v. *Trim-Lok, Inc.*, 869 F.3d 1372, 1381 (Fed. Cir. 2017) (emphasis in original) (citation omitted); see also *Commil*, 135 S.Ct. at 1926 ("[C]ontributory infringement requires knowledge of the patent in suit and knowledge of patent infringement." (citation omitted)). The patentee bears the burden of proving infringement by a preponderance of the evidence. See *Octane Fitness, LLC* v. *ICON Health & Fitness, Inc.*, 572 U.S. 545, 134 S.Ct. 1749, 1758, 188 L.Ed.2d 816 (2014); *Seal–Flex, Inc.* v. *Athletic Track & Ct. Constr.*, 172 F.3d 836, 842 (Fed. Cir. 1999).

b. *Induced Infringement By Pfizer*

i) Parties' Contentions

The jury found that Pfizer has not "actively induced healthcare professionals and/or patients to directly infringe the asserted claims of the '755 patent." Verdict Form at 3, Q. 6. Biogen seeks to overturn the verdict of no induced infringement by emphasizing the jury's direct

infringement and contributory infringement verdicts. Specifically, Biogen argues that in finding direct infringement, the jury inherently found that Rebif® (interferon-β) treats MS through immunomodulation, an element of claim 1, because MS is indisputably an autoimmune disease and is not a viral condition, a viral disease, a cancer, or a tumor. See Biogen Br. at 23 (citing 1/29/18 AM Tr. at 102:22-103:21 (Kinkel)); 6/6/18 Tr. at 238:8-10; see also PTX0001 ('755 patent) at 49:59-60 ("A method for immunomodulation *or* treating a viral condition[ ], a viral disease, cancers or tumors . . . ." (emphasis added)). Biogen also contends that in finding contributory infringement, the jury necessarily found that Pfizer "*knew* that Rebif was being used by healthcare professionals and/or patients *in a manner that infringes* a claim of the '755 patent" and that "Rebif has no substantial, non-infringing use." Final Jury Instructions at 24 (emphasis added); see also 6/6/18 Tr. at 238:15-21. Biogen argues that, when considered together, these two findings indicate that the jury agreed with Biogen that Pfizer knows how Rebif® works and that Pfizer knows it works through immunomodulation. According to Biogen, with respect to inducement, the only question remaining for the jury to decide was whether Pfizer *intended* for Rebif® to work through immunomodulation. See Final Jury Instructions at 22 (instructing jury that to be liable for induced infringement, Pfizer must have "specifically intend[ed] to cause the infringing acts by healthcare professionals and/or patients").

In Biogen's view, the verdict in Pfizer's favor cannot stand because no reasonable jury could have concluded that Pfizer lacked the specific intent to induce infringement. Biogen contends that the jury heard ample evidence that Pfizer had the specific intent to induce the di-

rect infringement of the '755 patent claims—i.e., Pfizer specifically intended that Rebif® be used to treat MS through immunomodulation, as opposed to through some other way. Biogen Br. at 21-27. In particular, Biogen cites the testimony of its expert Dr. Kinkel, who opined that there is a consensus in the scientific community that Rebif® works through immunomodulation to treat MS. *Id.* at 23 (citing 1/29/18 AM Tr. at 121:11-17, 127:6-9; 1/29/18 PM Tr. at 33:25-34:7). Biogen also cites as proof that Pfizer intends that Rebif® works through immunomodulation an internal Pfizer presentation entitled "Rebif Business Review," which characterizes Rebif® and other interferon-β products as "immunomodulatory agents" (PTX0659 at 87), and diagrams the "MOA" (mechanism of action) of interferon-β in treating MS as modulating the immune response (*id.* at 14). Biogen Br. at 24-25; see also 1/29/18 PM Tr. at 32:18-33:24 (Kinkel). Biogen further cites the Rebif® Biologics License Application ("BLA"), submitted to the United States Food and Drug Administration ("FDA"), which identifies three proposed mechanisms of action for interferon-β "in influencing MS disease," all of which "result in modulation of the immune process, which leads to reduction in disease activity," (PTX0059 at 163), and states that interferon-β "exerts a number of immunoregulatory effects on cells of MS patients" and "seems to act by regulating excessive immune responses in the local inflammation sites in MS," (PTX0061 at 19-20). Biogen Br. at 25-26; see also 1/29/18 PM Tr. at 23:17-24:18 (Kinkel). Biogen also cites the testimony of Defendants' expert Dr. Gutterman, who agreed that it was known that interferon-β is immunomodulatory, may play a role in the regulation of the immune response, and can be both immunopotentiating and immunosuppressant depending on the time and dose of application. See 2/7/18 PM Tr. at 36:25-37:4, 45:6-13, 46:16-19.

Biogen contends that Defendants failed to present any rebuttal fact or expert testimony regarding—or any alternative, non-immunomodulatory hypothesis for—how Rebif® works to treat MS to support a verdict that Pfizer lacked the requisite intent. See 6/6/18 Tr. at 239:1-6. Thus, in Biogen's view, no reasonable jury could conclude that Pfizer did not intend that Rebif® be used for immunomodulation in the treatment of MS.

Defendants nevertheless contend that the Court should not disturb the verdict of no inducement by Pfizer. Defendants reiterate that it is Biogen, not Defendants, who bore the burden of proving inducement. Defs. Opp. at 22. While Defendants do not dispute that interferon-β has immunomodulatory properties, in their view, "Biogen had to prove that [Defendants] specifically intended immunomodulation to be that mechanism of action" by which interferon-β treats MS. 6/6/18 Tr. at 258:7-15. To support the jury's finding that Pfizer lacked the specific intent to induce infringement, Defendants cite the Rebif® package insert label, which states that the "mechanism(s) by which REBIF (interferon beta-1a) exerts its therapeutic effects in patients with multiple sclerosis is unknown," (PTX0582 at 11), and Dr. Kinkel's testimony that "all of the labels for the FDA-approved interferon beta drugs, [Biogen's interferon-β product] Avonex included, state that the mechanism of action is unknown" (1/29/18 PM Tr. at 49:16-50:5, 55:18-56:2). Defs. Opp. at 23. Defendants characterize this evidence as proof that it is unknown whether the various immunomodulatory properties of interferon-β work to treat MS, and that Biogen's cited evidence "actually emphasizes the uncertainty in the field as to what causes MS and how IFN-β treats it." *Id.* at 22. Defendants also rely on the testimony of Giampiero De Luca, Serono's former Chief Intellec-

tual Property Counsel, in which he questions whether patients know that interferon-β immunomodulates when it treats MS. *Id*. at 23 (citing 8/15/12 De Luca Dep. Tr. at 168:25-169:6, 169:13-23). Defendants argue that the jury was entitled to credit this testimony and evidence and conclude that Biogen failed to meet its burden of establishing Pfizer's specific intent.

ii) Biogen Is Entitled to JMOL of Induced Infringement By Pfizer

Having reviewed the record under the appropriate standard, including drawing all reasonable inferences in favor of Defendants as the non-movants, the Court concludes that no reasonable jury could have found that Pfizer lacked the specific intent to induce infringement. In reviewing the entirety of the record evidence, the Court has "give[n] credence to the evidence favoring" Defendants as well as evidence supporting Biogen that is "uncontradicted and unimpeached." *Reeves*, 530 U.S. at 151, 120 S.Ct. 2097; *Integra Lifesciences*, 496 F.3d at 1345.

Whether Pfizer "took action after the time the '755 patent issued specifically intending to cause the infringing acts by healthcare professionals and/or patients" is the only element in the inducement inquiry that does not overlap with direct or contributory infringement. Final Jury Instructions at 22. Defendants' argument in support of the inducement verdict, which relies primarily on the language in the Rebif® label and other interferon-β product labels, goes to a different question that the jury resolved *against* Pfizer. Specifically, in finding contributory infringement, the jury rejected Defendants' argument that Pfizer does not know that Rebif® works

through immunomodulation to treat MS.[19] Moreover, the language in the interferon-β product labels cited by Defendants regarding interferon-β's mechanism of action is far outweighed by and, in fact, is consistent with the record evidence of intent; what is "unknown" is only the *precise* mechanism(s) involved. See 1/29/18 AM Tr. at 122:21-23 (Kinkel) ("A mechanism of action is the precise way that a particular drug has its effect."). When asked: "[I]s there any serious debate in the scientific community about whether interferon-βeta is immunomodulatory in treating multiple sclerosis?" Dr. Kinkel answered: "No, there is not." *Id.* at 127:6-9. While it is true that the jury may disregard evidence on disputed propositions, see *Reeves*, 530 U.S. at 151, 120 S.Ct. 2097, here there was no contrary testimony or evidence that the jury could have credited over this testimony. Although Defendants do not bear the burden of proving noninfringement, no fact or expert witnesses testified that Pfizer lacked specific intent or to "any degree of agnosticism or ignorance or skepticism on the part of Pfizer." 6/6/18 Tr. at 285:25-286:1. No contrary hypothesis was advanced or was supported by the record. In the absence of contrary evidence, the jury was not free to disregard the evidence of Pfizer's intent proffered by Biogen. Therefore, no reasonable jury could have concluded that Pfizer did not intend that Rebif® be used to treat MS through immunomodulation.

---

[19] The only other purportedly supportive evidence Defendants cite is Mr. De Luca's testimony. Defendants have not pointed to any evidence in the record showing that Pfizer was aware of or was influenced by *Serono* principal Mr. De Luca's statements, nor have they provided a sufficient explanation as to how his testimony bears on *Pfizer's* state of mind.

Accordingly, the Court grants Biogen's Rule 50(b) JMOL motion as to induced infringement by Pfizer and vacates the jury's verdict in favor of Pfizer. For the same reasons that the Court grants Biogen's JMOL motion, the Court concludes that the jury's verdict is against the clear weight of the evidence and conditionally orders a new trial on induced infringement by Pfizer pursuant to Rule 50(c)(1). Biogen's alternative request for a new trial under Rule 59 is denied as moot.

c. *Induced Infringement By Serono*

i) Parties' Contentions

The jury found that Serono has not "actively induced healthcare professionals and/or patients to directly infringe the asserted claims of the '755 patent." Verdict Form at 2, Q. 2. As with Pfizer, Biogen seeks to overturn the verdict of no induced infringement by emphasizing the jury's direct infringement and contributory infringement verdicts. The Verdict Form, as prepared and supplied by the parties, included the following four questions with regard to Serono's alleged inducement, which have been conformed to show the jury's response:

> 2. Do you find, by a preponderance of the evidence, that Serono has actively induced healthcare professionals and/or patients to directly infringe the asserted claims of the '755 patent?
>
> Yes __ (for Biogen)
>
> No ✓ (for Serono)
>
> *If your answer to Question 2 is "Yes", continue to Question 3. If your answer is "No", do not continue to Question 3, but instead proceed to Question 6.*
>
> 3. Do you find, by a preponderance of the evidence, that it is. unreasonable to read the '755 patent claims to require three steps (transformation of the

nonhuman host cell, production of the recombinant polypeptide, and administration) as opposed to only a single step (of administration)?

Yes __ (for Biogen)

No __ (for Serono)

4. Do you find, by a preponderance of the evidence, that for at least some time period Serono lacked a good faith belief that its acts did not induce direct infringement of the asserted claims of the '755 patent?

Yes __ (for Biogen)

No __ (for Serono)

5. If you find that Serono lacked a (1) reasonable and (2) good faith belief that its acts did not induce direct infringement, over what span of time do you find that Serono lacked such a belief?

Please specify: _____

Verdict Form at 2. The Verdict Form instructed the jury to skip Questions 3, 4, and 5 if it answered "No" to Question 2. *Id.* The jury answered "No" to Question 2 and left blank Questions 3, 4, and 5, which address whether Serono reasonably believed in good faith that the '755 patent claims require three steps (transformation of the non-human host cell, production of the recombinant polypeptide, and administration to a patient), a proposed construction that the Court rejected during claim construction.[20] See *Markman* Op. at 17 (construing claim 1 as reciting a "one-step method of 'administering' to a patient in need the specified recombinant HuIFN-β").

---

[20] Defendants did not advance a reasonable, good-faith belief defense in response to Biogen's inducement claim against Pfizer.

As with the jury's inducement verdict in favor of Pfizer, Biogen contends that the jury's verdict of no inducement by Serono cannot stand because no reasonable jury could have concluded that Serono lacked the specific intent to induce infringement. In Biogen's view, the jury's answer of "No" to Question 2 indicates that it ruled on Defendants' immunomodulation theory as it did for Pfizer, and did not reach Serono's reasonable, good-faith belief defense. Biogen contends that the latter theory cannot support a verdict of no inducement in any case, given that Serono conceded during trial that it relinquished its belief of noninfringement following the Court's March 28, 2016 claim construction ruling. ECF No. 1003 ("Biogen Reply") at 12-13; 6/6/18 Tr. at 247:8-9, 248:4-18, 250:8-12, 287:21-288:21. With respect to Defendants' immunomodulation theory, Biogen argues that in finding contributory infringement by Serono, as it did with Pfizer, the jury rejected Defendants' argument that Serono does not know that Rebif® works through immunomodulation to treat MS. As affirmative evidence supporting an inducement finding, Biogen cites (i) the Rebif® BLA's sections that Biogen cited in challenging the inducement verdict for Pfizer; (ii) Serono's internal presentation entitled "Interferon-β Pharmacokinetics, Pharmacodynamics and Mechanism of Action," which recounts seven facets of "Immunomodulatory Activity of IFN" and diagrams how interferon-β affects the immune response in MS (PTX0227 at 26-29); (iii) an article by Dr. Revel, who was involved in the development of Rebif® on behalf of Serono, entitled Interferon-β in the treatment of relapsing-remitting multiple sclerosis, Pharmacol Ther. 100(*l*):49-62 (2003), which states that the "anti-inflammatory and immunomodulatory effects of interferon-β are the predominant mechanisms responsible for its effectiveness as a MS [disease-modifying drug]" (PTX1055 at 4); and (iv)

Serono's failure to call an expert witness to present any alternative, non-immunomodulatory hypothesis for interferon-β's mechanism of action in treating MS. Biogen Br. at 31-32.

In response, Defendants assert that sufficient evidence supports the verdict of no inducement by Serono. Specifically, Defendants contend that the jury heard evidence that Serono (i) did not believe that interferon-β treats MS through immunomodulation, based on the same evidence discussed above with respect to Pfizer's intent, including the testimony of Mr. De Luca; and (ii) reasonably believed that the '755 patent claims require multiple steps that Serono never carried out, based on the independent assessments of the claims by Mr. De Luca and Henry Einav, the latter an Israeli patent attorney employed by, and responsible for patent prosecution and patent licensing for, Serono (2/8/18 AM Tr. at 7:12-14, 8:16-25 (Einav)), and the advice of United States patent attorneys Roger Browdy and John White. Defs. Opp. at 23-27. In Defendants' view, Question 2 of the Verdict Form is not limited to any particular noninfringement theory. Defendants also contend that, contrary to Biogen's assertion, Serono did not relinquish its belief in noninfringement after the Court's claim construction decision, and the jury could have concluded that Serono's belief was reasonable. 6/6/18 Tr. at 265:9-18, 267:6-10. According to Defendants, a reasonable jury considering this evidence could have concluded that Biogen failed to meet its burden of establishing that Serono specifically intended to cause direct infringement.

ii) Biogen Is Entitled to JMOL of Induced Infringement By Serono

Having reviewed the record under the appropriate standard, including drawing all reasonable inferences in

favor of Defendants as the non-movants, the Court concludes that no reasonable jury could have found that Serono lacked the specific intent to induce infringement. As discussed above with respect to Pfizer, by finding direct infringement of the '755 patent claims, the jury found that Rebif® treats MS through immunomodulation. By finding that Serono contributed to the infringement of the '755 patent claims, the jury necessarily found that Serono "*knew* that Rebif was being used by healthcare professionals and/or patients *in a manner that infringes* a claim of the '755 patent" and that "Rebif has no substantial, noninfringing use." Final Jury Instructions at 24 (emphasis added). As discussed above with respect to Pfizer, because no other mechanism of action was suggested in the record, the jury could not therefore have reasonably inferred any other mechanism of action by which Rebif® treats MS. Accordingly, JMOL of inducement against Serono is appropriate because no reasonable jury could have concluded that Serono did not intend that Rebif® be used for immunomodulation in the treatment of MS.

The Court therefore turns to Defendants' other basis to uphold the verdict. As discussed above, the parties offer competing interpretations of Verdict Form Questions 2 through 5. On the one hand, Biogen reads the jury having not answered Questions 3, 4, and 5 as showing that the jury did not reach the issue of Serono's reasonable, good-faith belief of noninfringement in making its determination of induced infringement. The jury was directed by the Verdict Form to answer Question 3, 4, and 5 *only if* it answered "Yes" to Question 2. See Verdict Form at 2. In other words, only if the jury found that Serono induced infringement did it then need to decide whether, and for what period of time, Serono had a valid

defense to rebut such a finding of liability. See *id.* On the other hand, under Defendants' reading of the Verdict Form, despite having not answered Questions 3, 4, and 5, the jury could have still considered Serono's reasonable, good-faith belief defense in answering Question 2 because that question includes no limitation as to the bases for finding (or not finding) liability for inducement.

The Court is disinclined to give credence to non-answers by the jury. In addition, the directive on the Verdict Form to bypass Questions 3, 4, and 5 essentially instructed the jury to only consider Serono's reasonable, good-faith belief defense in the event it found that Serono had actively induced infringement. However, even if the Court were to agree with Defendants' interpretation of the Verdict Form—that the jury did, in fact, conclude that Serono did not induce infringement because the jury found that Serono held a reasonable, good-faith belief in noninfringement—the jury's verdict still cannot stand because it is not supported by substantial evidence. The jury heard evidence that as of March of 2016, when the Court issued its claim construction decision construing claim 1 as a one-step method, Serono no longer believed in its three-step claim construction. See 2/8/18 AM Tr. at 73:11-74:21 (Einav); 2/8/18 PM Tr. at 15:4-21 (Einav) (testifying that prior to the Court's claim construction ruling, Serono "believed for all that time that we are talking about a three-step process," and that subsequent to the Court's claim construction it acknowledged that this ruling "is the law and this is what we accept and this is what we understand"). Thus, substantial evidence does not support a finding that Serono held its belief of noninfringement at all times following the issuance of the '755 patent on September 15, 2009.

Accordingly, the Court grants Biogen's Rule 50(b) JMOL motion as to induced infringement by Serono and vacates the jury's verdict in favor of Serono. For the same reasons that the Court grants Biogen's JMOL motion, the Court concludes that the jury's verdict is against the clear weight of the evidence and conditionally orders a new trial on induced infringement by Serono pursuant to Rule 50(c)(1). Biogen's alternative request for a new trial under Rule 59 is denied as moot.

3. *Invalidity Defenses Not Litigated*

a. *Applicable Legal Principles*

"Under Rule 50, a court should render judgment as a matter of law when 'a party has been fully heard on an issue and there is no legally sufficient evidentiary basis for a reasonable jury to find for that party on that issue.'" *Reeves*, 530 U.S. at 149, 120 S.Ct. 2097 (quoting Fed. R. Civ. P. 50(a)). "A court should not render judgment with respect to claims 'reference[d] in the complaint' but not raised in the pretrial statement or litigated at trial; 'a reference in the complaint is not sufficient to support a judgment.'" *Alcon Research Ltd.* v. *Barr Labs., Inc.*, 745 F.3d 1180, 1193 (Fed. Cir. 2014) (quoting *800 Adept, Inc.* v. *Murex Sec., Ltd.*, 539 F.3d 1354, 1367-68 (Fed. Cir. 2008)).

"While waiver, as a general principle, is not unique to patent law," courts in the Third Circuit have applied Federal Circuit precedent to the question of whether a patent-law-specific defense is waived. See, *e.g.*, *Cubist Pharms., Inc.* v. *Hospira, Inc.*, 75 F.Supp.3d 641, 673-74 (D. Del. 2014); *Allergan Inc.* v. *Barr Labs., Inc.*, 808 F.Supp.2d 715, 735 (D. Del. 2011), aff'd, 501 F. App'x 965 (Fed. Cir. 2013). Courts in other circuits also apply Federal Circuit precedent to evaluate the waiver of validity defenses in patent cases. See, *e.g.*, *Asetek Danmark A/S*

v. *CMI USA, Inc.*, 100 F.Supp.3d 871, 892 (N.D. Cal. 2015); *Fractus, S.A.* v. *Samsung Elecs. Co.*, 876 F.Supp.2d 802, 838 (E.D. Tex. 2012).

b. *Parties' Contentions*

Biogen seeks a judgment as to certain affirmative defenses that Defendants included in their Answers but purportedly "discarded" at trial: (1) obviousness-type double patenting; (2) anticipation based on United States Patent No. 5,460,811 (the "Goeddel patent"); and (3) improper inventorship under 35 U.S.C. §§ 116, 256.[21] Biogen contends that while Defendants maintained these invalidity defenses after the December 13, 2017 deadline by which to withdraw claims and defenses, Defendants did not present evidence or otherwise pursue these defenses at trial. Biogen Br. at 33; ECF No. 1011 at 1. According to Biogen, JMOL is warranted because having pled and maintained these defenses, Defendants were obligated to (and ultimately failed to) prove them by clear and convincing evidence at trial. Biogen Br. at 34; 6/6/18 Tr. at 298:21-23 ("[Defendants] lose on the merits for their failure to prove an issue as to which they bear the burden. They chose not to do it."). Biogen contends that in any future trial on liability, Defendants "cannot then decide to raise these defenses which they deemed not good enough to make the cut the first time." ECF No. 1011 at 1.

---

[21] Biogen also seeks JMOL on Defendants' defense of patent ineligibility under 35 U.S.C. § 101. The Court addresses Biogen's JMOL motion with respect to Defendants' defense of patent ineligibility in Section III.B.1 below. Although Defendants raised their defense of patent ineligibility on a Rule 50(a) JMOL motion before the verdict, Defendants did not seek JMOL as to improper inventorship, obviousness-type double patenting, or anticipation based on the Goeddel patent.

In response, Defendants concede that they did not present any evidence in support of these defenses at trial. However, Defendants contend that Biogen's request is inappropriate because a Rule 50 JMOL motion is limited to issues on which "a party has been fully heard . . . during a jury trial." Defs. Opp. at 28 (quoting Fed. R. Civ. P. 50(a)(1)). According to Defendants, Biogen improperly seeks an advisory opinion on issues that were not litigated. *Id.* Defendants contend that while they "will live with whatever the consequences are of [the] fact" that they chose not to actively litigate their defenses at trial "should there be another liability trial in this matter," there is "no reason for the Court to decide now that [Defendants] waived these invalidity defenses." ECF No. 1017 at 2 (emphasis in original). Defendants contend that their defenses are not yet ripe for adjudication and "may never become ripe," and that the "legal effect of not pursuing these defenses will be determined if and when it becomes relevant." *Id.*

c. *Defendants Waived Their Non-Litigated Defenses*

Given that Defendants had the opportunity to either present evidence on their invalidity defenses or else withdraw these defenses, and yet chose inaction, a finding of waiver is appropriate. See *Acorda Therapeutics, Inc.* v. *Roxane Labs., Inc.*, No. 14-882, 2017 WL 1199767, at *28 (D. Del. Mar. 31, 2017) (concluding that the defendants' enablement and written description defenses "could likely be found to have been waived" where "none of the experts testified at trial" about those defenses); *Asetek*, 100 F.Supp.3d at 891-94 (finding waiver of written description and indefiniteness defenses where the defendant "adduced no evidence on" those defenses at trial); *Fractus*, 876 F.Supp.2d at 838-39 (finding that the

defendant waived its indefiniteness argument by failing to present testimony or other evidence in support of the defense at trial).

The Federal Circuit has explained that "[i]t is a claimant's burden to keep the district court clearly apprised of what parts of its claim it wishes to pursue and which parts, if any, it wishes to reserve for another day." *Silicon Graphics, Inc.* v. *ATI Techs., Inc.*, 607 F.3d 784, 801 (Fed. Cir. 2010). Here, "it was incumbent on [Defendants] to expressly request" that the Court "dismiss [their defenses] without prejudice." *Id.* Defendants did not notify the Court to withdraw or request dismissal of these defenses, with or without prejudice. Defendants did not notify Biogen of the withdrawal of any of these defenses, despite the deadline set forth in the pretrial schedule. ECF No. 866 at 5. Although Defendants joined Bayer's Motion for Summary Judgment of Invalidity No. 4 (Anticipation by the Goeddel Patent), (see ECF Nos. 513, 531), which the Court denied, (Summ. J. Op. at 35), waiver has been found in similar circumstances where a party has declined to pursue defenses at trial after denial of summary judgment on those defenses. See *Lisle Corp.* v. *A.J. Mfg. Co.*, 398 F.3d 1306, 1317 (Fed. Cir. 2005). Moreover, Defendants do not appear to cite cases permitting a defendant to seek to assert defenses they elected not to prove in a first trial. Because Defendants had a full chance to pursue these defenses at trial, they will be held to have waived them. See *Silicon Graphics*, 607 F.3d at 801 (affirming decision to deem invalidity counterclaims not pursued at trial as "withdrawn or abandoned" where the defendants did not explain how it would serve judicial economy to permit them to "keep their untried claims alive").

The Court also finds in the alternative that, even if Defendants had not waived their defenses of obviousness-type double patenting and anticipation by the Goeddel patent, Defendants failed to present clear and convincing evidence that the '755 patent claims are invalid on either of those two grounds. The Court has "assessed both what the parties expected to try given their statements and conduct and what they actually litigated at trial." *Alcon Research*, 745 F.3d at 1193. The parties' pretrial submissions demonstrate that Defendants placed certain defenses at issue for the trial. For instance, the Joint Pretrial Statement lists anticipation and obviousness-type double patenting as "joint issues of fact to be litigated."[22] ECF No. 916 at 10-11. Defendants' Trial Brief similarly contends that the '755 patent claims are anticipated by the Goeddel patent. ECF No. 901 at 2. In addition, Dr. Lodish listed "Anticipation by the Goeddel patent" among the eight topics of his testimony, and said "we'll come to [it] later," (2/8/18 PM Tr. at 50:15-51:3), but did not offer testimony about the defense. Although Defendants appeared to put obviousness-type double patenting and anticipation by the Goeddel patent at issue, Defendants did not include these defenses in the Final Jury Instructions or Verdict Form. Defendants failed to present any evidence in support of these defenses at trial for the jury to consider.

Contrary to Defendants' assertion, *Alcon Research* does not preclude the Court deciding the merits of their non-litigated defenses. In *Alcon Research*, the defendant sought JMOL of noninfringement for two patents where

---

[22] Anticipation is a question of fact, *In re Hodges*, 882 F.3d 1107, 1111 (Fed. Cir. 2018), and obviousness-type double patenting is a question of law based on underlying factual inquiries, *Eli Lilly & Co.* v. *Teva Parenteral Meds., Inc.*, 689 F.3d 1368, 1376 (Fed. Cir. 2012).

the plaintiff "neither put forward evidence of infringement nor formally obtained a dismissal of the claims involving those patents from its complaint prior to trial." 745 F.3d at 1192. The district court denied the defendant's JMOL motion, finding that "the claims regarding the [two] patents were no longer in the case as of the time of the trial and . . . essentially deeming [the plaintiff's] complaint as amended to remove them." *Id.* at 1193. Notably, the plaintiff had informed the defendant before trial "of its decision to drop its claims" for those patents, the defendant "subsequently omitted them from the pretrial order," and those patents were not litigated "or fairly placed in issue" at trial. *Id.*

Unlike the plaintiff in *Alcon Research*, Defendants (i) did not provide pre-trial notice to their adversary that they were withdrawing any of the challenged defenses; and (ii) included their obviousness-type double patenting and anticipation by the Goeddel patent defenses in their pretrial submissions to the Court. *Alcon Research* does not appear to preclude the entry of JMOL where a defendant chooses not to adduce evidence in such circumstances. Indeed, courts have stated that entry of judgment would be appropriate in these circumstances. See, *e.g.*, *Innogenetics, N.V.* v. *Abbott Labs.*, 512 F.3d 1363, 1371 (Fed. Cir. 2008) (affirming entry of JMOL of literal infringement where the defendant was deemed "fully heard on the issue of literal infringement" as the defendant had forfeited its noninfringement argument by not raising the issue sufficiently in advance of the start of trial and there was "no legally sufficient evidentiary basis for a reasonable jury to find for [the defendant] on that issue"); *Acorda*, 2017 WL 1199767, at *29 (concluding that "assuming the defenses have not been waived, Defendants have failed to meet their burden to prove, by

clear and convincing evidence, that the [patent-in-suit] is invalid due to lack of enablement or written description"); *Asetek*, 100 F.Supp.3d at 893-94 (noting that where the defendant listed indefiniteness in its pre-trial papers but did not litigate its indefiniteness defense at trial, even absent waiver, the court "would be compelled to find that [the defendant] did not carry its burden to prove, by clear and convincing evidence, that [the] patents are invalid for indefiniteness"); *Fractus*, 876 F.Supp.2d at 838-39 (concluding that where the defendant listed its indefiniteness defense in the pretrial order but "failed to present any explicit indefiniteness evidence at trial" and "failed to make a single reference to indefiniteness during trial," even absent waiver, the defendant failed to present clear and convincing evidence on the defense). The issues of whether the '755 patent claims are invalid for obviousness-type double patenting and anticipation by the Goeddel patent were "fairly placed in issue," and were not akin to the infringement claims in *Alcon Research* that were merely "referenced in the complaint" and later withdrawn. Accordingly, the Court agrees with Biogen that "[h]aving pleaded and maintained" these defenses, "Defendants bore the burden of proving them by clear and convincing evidence" and "failed to do so." Biogen Br. at 34.

With respect to Defendants' improper inventorship defense, as with their defenses of obviousness-type double patenting and anticipation by the Goeddel patent, Defendants pled this defense in their Answers but did not request a jury instruction or Verdict Form question on this defense, did not move for JMOL on this defense, did not seek to withdraw this defense before trial, and did not present any evidence of this defense during trial. Unlike the other challenged defenses, however, Defend-

ants did not identify their inventorship defense in the Joint Pretrial Statement or their Trial Brief. Given that Defendants did not raise this defense in their pretrial submissions and did not otherwise pursue this defense in the case, the Court considers Defendants' improper inventorship defense abandoned but finds that an entry of judgment on this defense based on an alleged failure of proof is inappropriate. See *Apple, Inc.* v. *Samsung Elecs. Co.*, 67 F.Supp.3d 1100, 1116-17 (N.D. Cal. 2014) (concluding that because the defendant "raised [certain] defenses in its Answer but did not raise them in the pretrial statement nor litigate them at trial," these defenses were "abandoned" but "no judgment may be rendered on these defenses" in favor of the plaintiff), aff'd, 816 F.3d 788 (Fed. Cir. 2016), vacated in part on reh'g en banc, 839 F.3d 1034 (Fed. Cir. 2016); *Silicon Graphics, Inc.* v. *ATI Techs., Inc.*, 573 F.Supp.2d 1108, 1113-14 (W.D. Wisc. 2008) (entering judgment in favor of the plaintiff with respect to only the defendants' invalidity counterclaims that were pursued at trial, but deeming "abandoned or waived" the remaining counterclaims "[b]ecause defendants had a full chance to try all of their claims of invalidity"), aff'd, 607 F.3d 784 (Fed. Cir. 2010).

In sum, the Court concludes that the defenses of obviousness-type double patenting, anticipation by the Goeddel patent, and improper inventorship that Defendants could have asserted against the '755 patent claims but did not litigate at trial, as indicated above, are deemed waived.

4. *Subsidiary Damages Issues*

a. *Applicable Legal Principles for Patent Damages*

A patent owner, upon a finding that a patent is infringed, is entitled to recover "damages adequate to

compensate for the infringement, but in no event less than a reasonable royalty." 35 U.S.C. §284. Having prevailed on liability, a patent owner may receive a reasonable royalty or lost profits. See *Asetek Danmark A/S* v. *CMI USA Inc.*, 852 F.3d 1352, 1362 (Fed. Cir. 2017). "To recover lost profits, a patent owner must prove a causal relation between the infringement and its loss of profits." *Georgetown Rail Equip. Co.* v. *Holland L.P.*, 867 F.3d 1229, 1240 (Fed. Cir. 2017) (internal quotation marks and citation omitted). In other words, the patent owner must show a reasonable probability that, "but for" the infringing activity, it would have made the additional profits enjoyed by the infringer. *Micro Chem., Inc.* v. *Lextron, Inc.*, 318 F.3d 1119, 1122 (Fed. Cir. 2003); *Mentor Graphics Corp.* v. *EVE-USA, Inc.*, 851 F.3d 1275, 1285 (Fed. Cir. 2017) ("[T]he fact finder's job is to determine what would the patent holder have made (what would his profits have been) if the infringer had not infringed."), reh'g en banc denied, 870 F.3d 1298 (Fed. Cir. 2017), cert. dismissed, No. 17-804, —— U.S. ——, 139 S.Ct. 44, 201 L.Ed.2d 1122, 2018 WL 3978434 (U.S. Aug. 17, 2018).

There is "no particular required method to prove but for causation" in patent cases. *Mentor Graphics*, 851 F.3d at 1284. One "useful, but non-exclusive" method to establish the patent owner's entitlement to lost profits is the test first articulated in *Panduit Corp.* v. *Stahlin Bros. Fibre Works, Inc.*, 575 F.2d 1152 (6th Cir. 1978). *Id.* (citation omitted). The *Panduit* test requires the patent owner to show: (1) demand for the patented product; (2) absence of acceptable non-infringing alternatives; (3) manufacturing and marketing capability to exploit the demand; and (4) the amount of profit it would have made. *Id.* at 1285 (citing *Panduit*, 575 F.2d at 1156). Once the patent owner makes a prima facie showing under *Pan-*

duit, it can be reasonably inferred that the lost profits claimed were caused by the infringing sales, and the burden shifts to the infringer to show that the inference is unreasonable for some or all of the lost sales. See *Rite-Hite Corp.* v. *Kelley Co.*, 56 F.3d 1538, 1545 (Fed. Cir. 1995) (en banc).

The Federal Circuit has instructed that the "but for" inquiry "requires a reconstruction of the market, as it would have developed absent the infringing product, to determine what the patentee 'would . . . have made.'" *Grain Processing Corp.* v. *Am. Maize-Prods. Co.*, 185 F.3d 1341, 1350 (Fed. Cir. 1999) (citation omitted). "[A] fair and accurate reconstruction of the 'but for' market also must take into account, where relevant, alternative actions the infringer foreseeably would have undertaken had he not infringed." *Id.* at 1350-51. Consistent with this standard, this Court instructed the jury that it "must take into account, where relevant, alternative actions that Serono would have undertaken had it not infringed." Final Jury Instructions at 43.

"The goal of lost profit damages is to place the patentee in the same position it would have occupied had there been no infringement." *Mentor Graphics*, 851 F.3d at 1285. The question of legal compensability is one "to be determined on the facts of each case upon mixed considerations of logic, common sense, justice, policy and precedent." *Altana Pharma AG* v. *Teva Pharms. USA, Inc.*, No. 04-2355, 2013 WL 12157873, at *6 (D.N.J. Jan. 11, 2013) (quoting *Rite-Hite*, 56 F.3d at 1546). While the availability of lost profits presents a question of law, *Rite-Hite*, 56 F.3d at 1544, whether acceptable non-infringing alternatives exist, which may reduce or preclude a lost profits damages award, presents a question of fact, *Minn. Mining & Mfg. Co.* v. *Johnson & Johnson Ortho-*

paedics, Inc., 976 F.2d 1559, 1577 (Fed. Cir. 1992) (citing *Radio Steel & Mfg. Co.* v. *MTD Prods., Inc.*, 788 F.2d 1554, 1556 (Fed. Cir. 1986)).

b. *Parties' Contentions*

The jury did not reach the damages questions on the Verdict Form because it found that the '755 patent claims were invalid as anticipated over the prior-art uses of native, human interferon-β. See Verdict Form at 5-6, Qs. 13-18. Rule 50(b) permits post-trial JMOL motions as to issues "not decided by a verdict." Fed. R. Civ. P. 50(b). Biogen requests that if the Court enters JMOL in its favor on anticipation, the Court should schedule a new trial on damages. In addition, Biogen asks that the Court either (1) enter judgment in its favor as to three subsidiary damages-related issues and conditionally grant a new trial under Rule 50(c); or (2) in the alternative, grant a new trial on all damages issues under Rule 59. Biogen Br. at 35.

With respect to the first subsidiary damages issue, in seeking JMOL, Biogen reiterates essentially the same argument it made in opposition to Defendants' motion for partial summary judgment as to Biogen's claim of lost profits. As discussed in the Court's Opinion denying Defendants' summary judgment motion, the parties' dispute with respect to Biogen's entitlement to lost profits damages concerns a Nonsuit and Option Agreement, entered into by Serono and Biogen in October of 2000 (STX-0166). ECF No. 884 at 2. That agreement gave Serono certain rights, including an option to obtain a license to the patent application that later issued as the '755 patent. Serono's option to obtain a license to the '755 patent was available to Serono when the '755 patent issued in September of 2009. It appears that, to date, Serono has not exercised its option, and the option remains available.

As it did on summary judgment, Biogen contends that exercising the option under the Nonsuit and Option Agreement is not an "alternative action," and that "licensed Rebif" is not a non-infringing alternative. Biogen Br. at 35-37. Biogen asserts that "the Federal Circuit and various district courts have rejected the notion that the mere right to take a license precludes recovery of lost profits." *Id.* at 36 (citations omitted). Biogen cites *Immersion Corp.* v. *HTC Corp.*, No. 12-259, 2015 WL 834209, at *5 (D. Del. Feb. 24, 2015) as an example where a court rejects as "inconsistent with the premise of the lost profits analysis" the argument that in the but-for world, infringement can be "factored out" by assuming that the infringer would have exercised a license to make the otherwise-infringing sales. Second, Biogen also seeks a judgment in its favor that Biogen had the "capacity to manufacture and sell enough product to meet demand if Defendants had not been taking Biogen's market share." Biogen Br. at 37-38. Third, Biogen seeks a judgment in its favor that Biogen sells Avonex®, Plegridy®, and Tecfidera® to Biogen U.S. Corp. and profits on those sales. *Id.* at 38-39.

In opposition, Defendants contend that none of Biogen's cited cases "involved a unilateral 'right' to participate in the market," and disagree with Biogen's interpretation of the *Immersion* court's decision, which, in Defendants' view, merely "rejected as 'too far' the argument that the defendant would have taken a license not only to the patents, but to non-infringing products as well." Defs. Opp. at 29 (citing *Immersion*, 2015 WL 834209, at *5). With respect to Biogen's capacity to meet demand, Defendants contend that the jury was free to discard or disbelieve Biogen's evidence. *Id.* With respect to Biogen's profits from sales to Biogen U.S. Corp., Defendants

contend that this argument was contradicted by the testimony of Biogen's Senior Director of Tax, Mr. Eric Tisch, that Biogen "sells only the drug substance for further processing" and that the "transfer price on which Biogen's $4.56 billion in purported lost profits depends is set unilaterally by Biogen MA Inc. to achieve tax benefits and could be changed at any time." *Id.* (citing 1/31/18 Tr. at 63:12-64:9, 80:19-82:14).

c. *Biogen Is Not Entitled to JMOL as to Subsidiary Damages Issues*

The Court declined to conclude on summary judgment that the Nonsuit and Option Agreement precludes Biogen's claim of lost profits as a matter of law. In particular, the Court determined that Serono's motion raised genuine issues of material fact that were appropriate for a jury's consideration. ECF No. 884 at 10-12. As observed in this Court's prior decision, other district courts faced with arguments similar to those Defendants raised have sent the issue to the jury for resolution. See *Cardiac Pacemakers, Inc.* v. *St. Jude Med., Inc.*, 418 F.Supp.2d 1021, 1038 (S.D. Ind. 2006), aff'd in part, rev'd in part and remanded, 576 F.3d 1348 (Fed. Cir. 2009); *GlobespanVirata, Inc.* v. *Texas Instruments, Inc.*, No. 03-2854, ECF No. 239 (D.N.J. Nov. 7, 2005). No new authority has been cited that would compel this Court to rule as a matter of law that Defendants' theory of lost profits is foreclosed.[23] Although the district court in *Im-*

[23] *Immersion Corp.* v. *HTC Corp.* involved a motion to exclude expert testimony as opposed to a summary judgment or JMOL motion. The license agreement at issue, if accepted, would have licensed the patents-in-suit as well as certain of the plaintiff's software. No. 12-259, 2015 WL 834209, at *3 (D. Del. Feb. 24, 2015). The plaintiff's damages expert's lost-profits opinion was based on a hypothetical "but for" world in which the defendant took a license to the patents *and* the plaintiff's non-patented software. The district court deter-

mersion questioned the correctness of a damages theory Biogen contends is similar to the one Defendants have advanced, noting that "no case accepting this sort of lost profits analysis" had been cited, the court also noted "[t]o be fair, there is also no case rejecting this sort of lost profits analysis." 2015 WL 834209, at *5 n.7. In addition, during the trial both sides presented evidence in support of their positions on the subsidiary damages issues raised in Biogen's motion, and the jury did not reach the question of damages. In light of the Court's rulings on the parties' JMOL motions, the issue of damages still remains for resolution. The Court finds that Biogen's alternative request of having a new jury decide all damages issues as part of determining the amount of damages is the most prudent course of action. Accordingly, the Court denies Biogen's Rule 50(b) JMOL motion as to the subsidiary damages issues and grants Biogen's alternative request for a new trial on all damages issues pursuant to Rule 59.

B. Defendants' Post-Trial Motions

Defendants move for JMOL under Rule 50(b) as to (1) patent ineligibility; (2) obviousness; (3) lack of enablement and lack of adequate written description; (4) contributory infringement by Pfizer; and (5) lost profits damages. The Court addresses each of Defendants' motions in turn. The Court also addresses Biogen's JMOL

---

mined that this opinion went "too far" and was "not a viable theory" because it included as recoverable lost profits "whatever profits would have been made if Defendants licensed the software." *Id.* at *5 (after citing the proposition that the Patent Act "protects the right to exclude, not the right to exploit," rejecting the expert's lost-profits analysis that "in essence, begins with the infringer taking a license, and then asks, what else would the infringer have bought from the patent holder?" (quoting *King Instruments* v. *Perego*, 65 F.3d 941, 949 (Fed. Cir. 1995))).

motion as to Defendants' patent-ineligibility defense, specifically, Biogen's contention that Defendants waived their defense and that, even absent waiver, Defendants' defense fails on the merits.

1. *Patent Eligibility (Defendants' and Biogen's Motions)*

   a. *Applicable Legal Principles for Patent Eligibility*

Section 101 of the Patent Act states that "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof" may obtain a patent. 35 U.S.C. § 101. This provision contains certain "implicit exceptions": laws of nature, natural phenomena, and abstract ideas. *Berkheimer* v. *HP Inc.*, 881 F.3d 1360, 1366 (Fed. Cir. 2018) ("Because patent protection does not extend to claims that monopolize the 'building blocks of human ingenuity,' claims directed to laws of nature, natural phenomena, and abstract ideas are not patent eligible." (quoting *Alice Corp. Pty. Ltd.* v. *CLS Bank Int'l*, 573 U.S. 208, 134 S.Ct. 2347, 2354, 189 L.Ed.2d 296 (2014))), denying en banc reh'g, 890 F.3d 1369 (Fed. Cir. 2018). As with enablement, obviousness, and indefiniteness, "whether a claim recites patent eligible subject matter is a question of law which may contain underlying facts." *Id.* at 1368 (citations omitted); see also *Aatrix Software, Inc.* v. *Green Shades Software, Inc.*, 882 F.3d 1121, 1128 (Fed. Cir. 2018), denying en banc reh'g, 890 F.3d 1354 (Fed. Cir. 2018).

In *Mayo Collaborative Services* v. *Prometheus Laboratories, Inc.*, 566 U.S. 66, 132 S.Ct. 1289, 182 L.Ed.2d 321 (2012), and as later reiterated in *Alice*, the Supreme Court established a two-step test to determine whether claimed subject matter is patent eligible under § 101: (1)

the court determines whether the claims at issue are directed to a patent-ineligible concept (i.e., a law of nature, a natural phenomenon, or an abstract idea) and, if so, (2) the court must "consider the elements of each claim both individually and 'as an ordered combination' to determine whether the additional elements 'transform the nature of the claim' into a patent-eligible application." *Alice*, 134 S.Ct. at 2355 (quoting *Mayo*, 566 U.S. at 77-79, 132 S.Ct. 1289). "While each step involves its own separate inquiry," they may "involve overlapping scrutiny of the content of the claims." *Interval Licensing LLC* v. *AOL, Inc.*, 896 F.3d 1335, 1342 (Fed. Cir. 2018) (quoting *Elec. Power Grp., LLC* v. *Alstom S.A.*, 830 F.3d 1350, 1353 (Fed. Cir. 2016)).

The Supreme Court has explained that laws of nature, natural phenomena, and abstract ideas are not patentable because "they are the basic tools of scientific and technological work," *Mayo*, 566 U.S. at 71, 132 S.Ct. 1289 (citation omitted), even if the claimed subject matter is "[g]roundbreaking, innovative, or even brilliant," *Ass'n for Molecular Pathology* v. *Myriad Genetics, Inc.*, 569 U.S. 576, 591, 133 S.Ct. 2107, 186 L.Ed.2d 124 (2013) ("*Myriad I*"). The Supreme Court has cautioned, however, that "too broad an interpretation of" ineligible subject matter "could eviscerate patent law" because "all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas." *Mayo*, 566 U.S. at 71, 132 S.Ct. 1289. Thus, with respect to the first step of the *Alice* inquiry, "it is not enough to merely identify a patent-ineligible concept underlying the claim; we must determine whether that patent-ineligible concept is what the claim is 'directed to.'" *Vanda Pharms. Inc.* v. *West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1134 (Fed. Cir. 2018) (quoting *Rapid*

Litig. Mgmt. Ltd. v. *CellzDirect, Inc.*, 827 F.3d 1042, 1050 (Fed. Cir. 2016)); see also *Internet Patents Corp.* v. *Active Network, Inc.*, 790 F.3d 1343, 1346 (Fed. Cir. 2015) ("Under step one . . . the claims are considered in their entirety to ascertain whether their character as a whole is directed to excluded subject matter.").

In addition, the Supreme Court has described the second step of the *Alice* inquiry as a search for an "inventive concept"—i.e., an element or combination of elements that is "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself." *Alice*, 134 S.Ct. at 2355 (quoting *Mayo*, 566 U.S. at 73, 132 S.Ct. 1289). The "inventive concept must be evident in the claims." *RecogniCorp, LLC* v. *Nintendo Co.*, 855 F.3d 1322, 1327 (Fed. Cir. 2017); see also *Alice*, 134 S.Ct. at 2357 ("[W]e must examine the elements of the claim to determine whether it contains an 'inventive concept.'"). The second step is satisfied when the claim limitations "involve more than performance of 'well-understood, routine, [and] conventional activities previously known to the industry.'" *Berkheimer*, 881 F.3d at 1367 (citation omitted). "[W]hether a claim element or combination of elements is well-understood, routine and conventional to a skilled artisan in the relevant field is a question of fact" that must be proven by clear and convincing evidence. *Id.* at 1368 (citing *Microsoft*, 564 U.S. at 95, 131 S.Ct. 2238); see also *Berkheimer*, 890 F.3d at 1371 (Moore, J., concurring) ("Because the patent challenger bears the burden of demonstrating that the claims lack patent eligibility . . . there must be evidence supporting a finding that the additional elements were well-understood, routine, and conventional." (internal citation omitted)). In addition, whether a "particular technology is well-understood, rou-

tine, and conventional goes beyond what was simply known in the prior art" and the "mere fact that something is disclosed in a piece of prior art, for example, does not mean it was well-understood, routine, and conventional." *Berkheimer*, 881 F.3d at 1369.

b. *Waiver of Defendants' Patent-Ineligibility Defense*

As a threshold matter, Biogen contends, that the Court need not reach the merits of Defendants' patent-ineligibility challenge on the ground that the defense, which allegedly rests on disputed facts, was never presented to the jury and is therefore waived. Biogen points out that while the Joint Pretrial Statement lists patent eligibility among the issues of law to be litigated, (ECF No. 916 at 13), and Defendants' Trial Brief similarly contends that the '755 patent claims are patent ineligible, (ECF No. 901 at 2), Defendants did not seek resolution before or during the trial of disputed facts upon which the defense rests.[24] Biogen Opp. at 8-11. Specifically, Biogen asserts that Defendants did not move for summary judgment on this defense, nor did they present this

[24] Biogen notes that, as a point of comparison, the factual inquiries underpinning Defendants' other legal defense of obviousness were included in the "Issues of Fact to be Litigated" section of the Joint Pretrial Statement and Defendants actively litigated that defense to the jury during the trial. See ECF No. 916 at 11; 6/6/18 Tr. at 182:14-183:3; *id.* at 192:18-24 (arguing that "by not putting anything in the Joint Pretrial Statement about the facts that might be implicated by the eligibility defense, that was a waiver"). In response, Defendants argue that by not listing the factual inquiries of their patent-ineligibility defense in the Joint Pretrial Statement, they were being transparent about their position as to the legal nature of the defense, and that Biogen could have listed any underlying factual inquiries of the defense in the "Issues of Fact to be Litigated" section of the Joint Pretrial Statement but chose not to. See 6/6/18 Tr. at 192:5-17, 213:23-214:9.

defense to the jury. Biogen further contends that Defendants' decision to raise their patent-ineligibly defense in a Rule 50(a) motion is prejudicial to Biogen because it deprived Biogen of the ability to develop a record to effectively respond to Defendants' arguments. See 6/6/18 Tr. at 187:15-19.

By contrast, Defendants contend that questions of law such as patent eligibility are "regularly vetted in a Rule 50 motion when not presented to the jury" and that any facts underlying the legal defense are undisputed. ECF No. 1017 at 3. In Defendants' view, the "Section 101 issue is a straightforward legal issue for the Court that can be determined on the face of the patent and the patent claims alone." 6/6/18 Tr. at 199:22-25; see also *id.* at 199:6-9 (disputing that there are "facts that need to be adjudicated in connection with" determining whether the claims are patent eligible). Defendants also point out that "well-known model jury instructions lack any mention of eligibility." ECF No. 1002 ("Defs. Reply") at 4; see also 6/6/18 Tr. at 197:15-18.

The Court declines to preclude Defendants from raising a patent-eligibility challenge based on an alleged waiver. Unlike their defenses of obviousness-type double patenting, anticipation by the Goeddel patent, and improper inventorship, Defendants moved under Rule 50(a) for JMOL as to patent ineligibility during trial. The cases Biogen cites do not appear to compel a finding of waiver under these circumstances, given that in those cases either the movant had not moved for JMOL during trial or its Rule 50(a) motion provided insufficient notice of the precise legal challenge, an argument that Biogen does

not appear to make.[25] Moreover, as Defendants note, "as a procedural matter, the Federal Circuit has observed frequently that § 101 disputes may be amenable to resolution on motions for judgment on the pleadings, motions to dismiss, or summary judgment." *TriPlay, Inc.* v. *WhatsApp Inc.*, No. 13-1703, 2018 WL 1479027, at *6 (D. Del. Mar. 27, 2018), reconsideration denied, 2018 WL 3545500 (D. Del. July 24, 2018); see also *Berkheimer*, 881 F.3d at 1368 (noting that "not every § 101 determination contains genuine disputes over the underlying facts material to the § 101 inquiry"); *Exergen Corp.* v. *Kaz USA, Inc.*, 725 F. App'x 959, 963-68 (Fed. Cir. 2018) (affirming denial of a post-trial motion of § 101 ineligibility and noting that no factual or legal issues regarding the defense were submitted to the jury);[26] *Chamberlain Grp., Inc.* v. *Techtronic Indus. Co.*, 315 F.Supp.3d 977, 986-90 (N.D.

---

[25] See *Erfindergemeinschaft UroPep GbR* v. *Eli Lilly & Co.*, 276 F.Supp.3d 629, 654 (E.D. Tex. 2017) (finding waiver of written-description theory where the defendant's "general statement" in its oral Rule 50(a) motion was "not sufficient to provide notice" to the plaintiff of the defendant's "entirely new theory"); *Asetek Danmark A/S* v. *CMI USA, Inc.*, 100 F.Supp.3d 871, 893-94 (N.D. Cal. 2015) (finding that the defendant waived indefiniteness defense based in part on the defendant's failure to seek JMOL on the defense during trial, which could have prompted the plaintiff to submit rebuttal evidence on the issue); *Fractus, S.A.* v. *Samsung Elecs. Co.*, 876 F.Supp.2d 802, 838-39 (E.D. Tex. 2012) (finding waiver where the defendant did not move for JMOL regarding indefiniteness at the close of its case-in-chief or at the close of the evidence and therefore deprived the plaintiff of the opportunity to substantively respond with its own testimony or evidence).

[26] The Court notes that in *Exergen Corp.* v. *Kaz USA, Inc.*, the defendant had "acquiesced in the district court's resolution of any underlying fact questions" of the § 101 determination and through the joint pretrial submission the parties "agreed that the district court may, in its discretion, opt to send fact issues to the jury or not." 725 F. App'x 959, 968 (Fed. Cir. 2018).

Ill. 2018) (addressing as a legal matter and denying a Rule 50(b) JMOL motion on § 101 ineligibility following jury trial). Furthermore, the parties agree that it is an open question as to whether the Seventh Amendment applies to the factual underpinnings of a patent-eligibility challenge. See 6/6/18 Tr. at 185:1-3, 197:18-22; Biogen Opp. at 9; *Exergen*, 725 F. App'x at 968.

Given these circumstances, the Court is disinclined to deny Defendants' motion on the ground that it is procedurally improper. The Court therefore addresses Biogen's alternative argument that, even if Defendants' defense were properly preserved, entry of JMOL that the '755 patent claims are patent eligible is appropriate because Defendants have not carried their burden of proving, by clear and convincing evidence, that the '755 patent claims are patent ineligible.

c. *Parties' Contentions on Patent Eligibility*

Defendants contend that the '755 patent claims are ineligible under 35 U.S.C. § 101 and therefore invalid. Defendants frame their patent-ineligibility defense as an issue of law for the Court to decide and contend that the Court can reach its decision based on the face of the '755 patent alone. 6/6/18 Tr. at 199:4-9, 199:22-25. With respect to the first step of the *Alice* inquiry, in Defendants' view, the claims "cover a natural phenomenon and abstract idea" because they are "directed to a method of treatment which uses the same IFN-β polypeptide as that found in nature to perform the same function that it performs in nature."[27] Defs. Br. at 1-2; see also 6/6/18 Tr. at 175:5-177:1. Relying on *In re BRCA1- & BRCA2-*

[27] During oral argument, Defendants indicated that all three categories of patent-ineligible subject matter apply. 6/6/18 Tr. at 224:21-225:8.

Based Hereditary Cancer Test Patent Litigation, 774 F.3d 755 (Fed. Cir. 2014) ("*Myriad II*") and *In re Roslin Institute (Edinburgh)*, 750 F.3d 1333 (Fed. Cir. 2014), Defendants contend that the fact that the claimed interferon-β protein to be administered is made recombinantly does not, standing alone, render it or its use patent eligible given that the recombinant and native interferon-β proteins share the same linear array of amino acids. Defs. Br. at 5-6. In addition, Defendants contend that the claims recite "abstract ideas" because they are "directed to the idea—but not any particular manner—of using a product of nature (recombinant human IFN-β) to perform the same function that it performs in nature (treating viral diseases)." *Id.* at 7 (citations omitted).

With respect to the second step of the *Alice* inquiry, Defendants assert that the claims do not contain an inventive concept because they add no improvement or anything else new in terms of treatment. *Id.* at 7-10. In Defendants' view, the concept of administering a therapeutically effective mount of a "preexisting polypeptide" to a patient in need of treatment for certain diseases does not render the claims patent eligible because "practitioners had long administered native human IFN-β to patients to treat these diseases." *Id.* at 1-2; see also Defs. Reply at 3 (arguing that the claims lack an inventive concept because they "provide no unconventional manipulation of or improvement to the known methods of treating viruses with IFN-β").

In response, Biogen argues that Defendants' § 101 challenge lacks legal support. With respect to the first step of the *Alice* inquiry, according to Biogen, method of treatment claims, including those involving the administration of naturally-occurring products, have consistently been held patent eligible. Biogen Opp. at 12-17.

Biogen also asserts that the claims exclude treatment with native interferon-β and are instead limited to treatment with recombinant interferon-β made in a non-human host, and thus "pose[ ] no Section 101 concerns." *Id.* at 6; see also *id.* at 14-16. Biogen further contends that there is no legal support for Defendants' proposition that a method of treatment with a manmade protein is ineligible for patenting if that protein is identical to a naturally-occurring protein, and that even if there were support for such a proposition, the undisputed trial evidence shows that the three-dimensional proteins of native and recombinant interferon-β are not identical. *Id.* at 16-17.

With respect to step two of the *Alice* inquiry, Biogen contends that a jury could have reasonably found based on the record evidence that determining whether recombinant interferon-β made in a non-human host had biological activity akin to that of the native protein and could thus be used as a therapeutic agent was anything but "routine and conventional." *Id.* at 2, 17-19. On this point, Biogen argues that the jury heard ample evidence that the "best molecular biologists labored—in a worldwide, round-the-clock race" to express recombinant interferon-β and to "prove that the expressed protein had biological activity like native interferon-βeta and thus could be used as a therapeutic treatment." *Id.* at 18 (citations omitted). In Biogen's view, "routine and conventional is a harder standard to meet than obvious," (6/6/18 Tr. at 219:7-8), and here, the jury heard ample evidence on, and rejected, Defendants' obviousness defense. Biogen Opp. at 19 ("[I]t is simply not possible for the subject matter of a patent claim to be both nonobvious but yet sufficiently well known to be 'routine and conventional.'"). Thus, according to Biogen, even if the evidence and arguments

Defendants raise in their JMOL motion were presented to the jury, a reasonable jury could conclude that Defendants failed to establish by clear and convincing evidence that the '755 patent claims are patent ineligible.

d. *The '755 Patent Claims Are Patent Eligible*

Under step one of the *Alice* inquiry, the Court determines whether the '755 patent claims are directed to a patent-ineligible concept. In doing so, the Court looks at the "focus" of the claims and their "character as a whole." *Elec. Power*, 830 F.3d at 1353. In addition, consistent with the parties' approach in their briefs, the Court "compare[s] the claims at issue with claims that have been considered in the now considerably large body of decisions applying § 101." *TriPlay*, 2018 WL 1479027, at *6 (citation omitted). Based on a review of the '755 patent claims and relevant case law, the Court concludes that the '755 patent claims are not directed to a patent-ineligible concept.

Underlying Defendants' patent-ineligibility argument is the premise that naturally-occurring interferon-β and recombinant interferon-β share the same linear sequence of amino acids. In Defendants' view, under *Myriad II* and *Roslin*, this shared amino-acid sequence alone renders recombinant interferon-β ineligible under § 101. See Defs. Br. at 6 (Defendants contending that "like the clones in *Roslin* and the DNA strands in *Myriad II*, the recombinant IFN-β whose use the '755 patent covers is an 'exact genetic cop[y] of patent ineligible subject matter' that is not 'distinct in any relevant way' from its native counterpart" (quoting *Roslin*, 750 F.3d at 1337, 1339)). In their brief, Defendants rely on the parties' agreed-to construction of the word "polypeptide" and contend, without apparent citation to the factual record, that the "linear sequence folds into the therapeutically

effective conformation the claims employ just as native IFN-β does in the body." *Id.* at 3. The Court already rejected this argument in its anticipation analysis at the summary judgment stage, see Summ. J. Op. at 28, and in Section III.A.1 of this Opinion, in concluding that the fact that native and recombinant interferon-β share the same amino-acid sequence (or primary structure) does not render them the same. The Court finds this argument unavailing in the patent-eligibility context as well. The '755 patent claims encompass not only the amino-acid sequence but also the three-dimensional structure of the polypeptide, including any attached carbohydrate groups, that is necessary for the polypeptide to display biological activity and be used in medical treatment as required by the claims. As discussed above with respect to Biogen's anticipation JMOL motion, the record evidence shows that the three-dimensional native and recombinant interferon-β proteins are not the same. See, *e.g.*, 2/9/18 Tr. at 87:24-88:7 (Lodish) (testifying that the InterPharm Study revealed differences in the structures of the sugars of native and recombinant interferon-β and that he "wouldn't call them identical"); 2/15/18 PM Tr. at 48:21-23 (Garcia) ("[R]ecombinant interferon beta is not identical to native interferon beta."); *id.* at 100:5-101:2 (explaining that the sugar groups of native and recombinant interferon-β are "not identical, because the enzymes and the machinery used to add and trim and process these glycosylations are different in the animal cells than they are in the human cells").

Moreover, there is a distinction in the case law with regard to the patentability of method of treatment claims on the one hand and product claims and claims directed to methods of diagnosis on the other. As discussed above, the '755 patent claims a *method* for immunomodu-

lation, or treating viral diseases, cancers, or tumors, by administering to a patient a "therapeutically effective amount" of a composition comprising a "recombinant" interferon-β polypeptide produced in a "non-human host" that had been "transformed by a recombinant DNA molecule." The Court previously construed claim 1 of the '755 patent as reciting a "one-step method of 'administering' to a patient in need the specified recombinant HuIFN-β." *Markman* Op. at 17. Recent decisions by the Supreme Court and Federal Circuit addressing § 101 in the contexts of genetics and medical treatment inform this Court's analysis. With respect to the distinction drawn in the case law between method of treatments claims and other types of claims and its impact on this case, this Court looks first to the Supreme Court's *Mayo* decision. The Supreme Court in *Mayo* held that a claim directed to a diagnostic method for "optimizing" the dosage of certain drugs by administering those drugs to a patient and measuring the level of metabolites in the blood, wherein the level of metabolites indicated whether to adjust the dosage, recited a natural law. 566 U.S. at 74-77, 132 S.Ct. 1289. The next year, the Supreme Court in *Myriad I* held that a "naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated." 569 U.S. at 580, 133 S.Ct. 2107. Importantly, the Supreme Court differentiated product claims (i.e., claims directed to physical things such as genetic material) from method claims, noting that "method claims" and "patents on new applications of knowledge about [particular] genes" were "not implicated by [its] decision." *Id.* at 595, 133 S.Ct. 2107.

Earlier this year, the Federal Circuit in *Vanda* examined the Supreme Court's *Mayo* and *Myriad I* decisions in determining the patent eligibility of a method of

treatment claim involving the step of "determining" with a genotyping assay, and then "administering" a certain amount of drug based on that determination in order to "treat a particular disease." 887 F.3d at 1134. Relying in part on the Supreme Court's distinction in *Myriad I* between method claims and claims to "naturally occurring" products, the Federal Circuit concluded that the claimed method of treatment was patent eligible under the first step of the *Alice* analysis. *Id.* at 1136. In addition, the Federal Circuit evaluated the method of treatment claims as a whole and determined that, unlike the claims in *Mayo*, the claims were "directed to a method of using" a drug to treat a particular disease rather than being "directed to" a natural relationship that occurs in the human body. *Id.* at 1135.

Defendants attempt to analogize claim 1 of the '755 patent to the claims at issue in *Mayo*, (6/6/18 Tr. at 230:12-25), but the claims in *Mayo* were directed to a diagnostic method and not to the application of a drug to treat a particular disease. While the *Mayo* claims recited a step of administering a drug to a patient, that step was performed in order to gather data about the natural relationships, and thus was ancillary to the overall diagnostic focus of the claims.[28] As the Federal Circuit recognized in *Vanda*, method of treatment claims (which *apply* natural relationships as opposed to being "directed to" them) were identified by the Supreme Court as not being implicated by its *Mayo* and *Myriad* decisions because they "confine their reach to particular applications." 887 F.3d

---

[28] For the same reasons, *Ariosa Diagnostics, Inc.* v. *Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015) and *Genetic Technologies Limited* v. *Merial L.L.C.*, 818 F.3d 1369 (Fed. Cir. 2016), which, like *Mayo*, involved claims to methods of diagnoses rather than methods of treatment, are inapposite.

at 1135; see also *CellzDirect*, 827 F.3d at 1049 (citing "treating headaches with aspirin" as an example of a patent-eligible claim); *Pernix Ireland Pain DAC* v. *Alvogen Malta Operations Ltd.*, No. 16-139, 2018 WL 2768655, at *2 (D. Del. June 8, 2018) ("A claim to a method of treating an illness is typically more than an expression of a natural law; if it were otherwise, pharmaceutical patents would be hard to come by, as most methods of treatment using pharmaceuticals consist simply of the administration of a drug that affects the human body in a manner that is dictated by laws of nature."). Moreover, on June 7, 2018, the PTO issued a Memorandum providing guidance on the examination of method of treatment claims in view of the Federal Circuit's *Vanda* decision. ECF No. 1010, Ex. 1. The Memorandum states that "'method of treatment' claims that practically apply natural relationships should be considered patent eligible," and that "it is not necessary for 'method of treatment' claims that practically apply natural relationships to include nonroutine or unconventional steps to be considered patent eligible under 35 U.S.C. §101." *Id.* at 2-3. While not binding on this Court, the PTO's guidance is nevertheless persuasive.

The method claims at issue in this case are thus also distinguishable from the claims held ineligible in *Myriad II* and *Roslin*. *Myriad II* and *Roslin* involved claims not to methods of treatment but rather to man-made, physical things that were identical to products of nature. For example, in *Myriad II*, the Federal Circuit held that the claimed single-stranded DNA primers, which had the same structure and function as naturally-occurring primers, were not patent eligible. 774 F.3d at 760. That same year, the Federal Circuit held unpatentable claims to a genetic copy of a naturally-occurring organism—

Dolly, a cloned sheep—because she "is an exact genetic replica of another sheep and does not possess 'markedly different characteristics from any [farm animals] found in nature.'" *In re Roslin*, 750 F.3d at 1337 (quoting *Diamond* v. *Chakrabarty*, 447 U.S. 303, 310, 100 S.Ct. 2204, 65 L.Ed.2d 144 (1980)). Here, the claims at issue are method of treatment claims, not claims to DNA or polypeptides. Moreover, as stated above, based on the record evidence no reasonable jury could conclude that the recombinant protein administered in the claimed method is identical to the protein found in nature.[29]

The Court has undertaken step one of the *Alice* inquiry as a legal issue based on a review of the '755 patent claims, as Defendants propose, and concludes that the claims are not directed to a patent-ineligible concept. Therefore, the Court need not reach step two of the *Alice* inquiry. See *Vanda*, 887 F.3d at 1134 ("If the claims are not directed to a patent ineligible concept at step one, we

---

[29] Defendants also cite *Boehringer Ingelheim Pharmaceuticals, Inc.* v. *HEC Pharm Co.*, in which a claim to administering a drug (DPP-I inhibitor) for treating and/or preventing metabolic diseases was held patent ineligible. No. 15-5982, 2016 WL 7177704, at *9 (D.N.J. Dec. 8, 2016). This Court notes that the *Boehringer* court itself rejected the defendants' characterization of the method claim at issue as a natural law like those in *Mayo*, holding instead that "the act of administering the DPP-IV inhibitor . . . is an abstract idea." *Id.* Here, Defendants have not persuaded this Court that claims to methods requiring the physical act of administering a drug to treat a patient are "abstract ideas," which the Federal Circuit has described as "methods which can be performed mentally, or which are the equivalent of human mental work." *CyberSource Corp.* v. *Retail Decisions, Inc.*, 654 F.3d 1366, 1371 (Fed. Cir. 2011). In any event, *Boehringer* pre-dates *Vanda* and the Federal Circuit's detailed discussion of the "distinction between method of treatment claims and those in *Mayo*." *Vanda Pharms. Inc.* v. *West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1135 (Fed. Cir. 2018).

need not address step two of the inquiry." (citation omitted)). Accordingly, the Court denies Defendants' Rule 50(b) JMOL motion and grants Biogen's Rule 50(b) JMOL motion on this defense.

Even if the Court were to proceed to step two of the *Alice* inquiry, for example, based on a finding that the '755 patent claims are directed to a product of nature, it would still deny Defendants' motion. The dispute at step two turns on whether the elements or combination of elements of the claims were "well-understood, routine, and conventional" as of June 6, 1980. The Court agrees with Biogen that the evidence presented at trial, even if not adduced for the specific purpose of establishing that step two was met, nonetheless bears on this question. See 6/6/18 Tr. at 218:14-220:1, 219:7-13; see also *Exergen Corp.* v. *Kaz USA, Inc.*, 172 F.Supp.3d 366, 367 (D. Mass. 2016) (denying judgment of invalidity under § 101 "with the benefit of the evidence presented at the well-litigated jury trial" and "[g]uided by the jury's verdict, and by the pleadings specific to th[e] case"), aff'd, 725 F. App'x 959 (Fed. Cir. 2018); *Internet Patents*, 790 F.3d at 1347 (noting that a "pragmatic analysis of § 101 is facilitated by considerations analogous to those of §§ 102 and 103 as applied to the particular case"). The Court has looked to the additional claim elements individually and as an ordered combination. The claims require methods of treatment using recombinantly-expressed interferon-β shown to have the biological activity like that of the native protein. The patent specification discloses the benefits of the claimed method over prior-art treatments using the native protein, see PTX0001 ('755 patent) at 4:10-13; 6:54-7:7, and does not state or even suggest that expressing a biologically-active protein sufficient for therapeutic use by employing recombinant DNA technology

was well-known, routine, or conventional. Moreover, as discussed in Section III.B.2 below, there is legally sufficient evidence in the record to support the jury's finding that the claimed method would not have been obvious to a person of ordinary skill in the art ("POSA") as of June 6, 1980 in view of the work of several scientists working at that time to express biologically-active recombinant interferon-β. See 2/20/18 AM Tr. at 82:17-83:1 (Green) (opining that since the "best people in the world" were "working day and night spending months and months" trying to produce biologically-active recombinant interferon-β, this would not have been "routine" to a POSA); see also 1/25/18 PM Tr. at 102:12-103:15 (Derynck); 2/5/18 Tr. at 136:17-137:21 (Taniguchi); 5/7/12 Goeddel Dep. Tr. at 79:24-80:18. Based on a review of the claims, the specification, and other evidence and testimony in the record, and guided by the jury's verdict on obviousness, the Court concludes that Defendants have not met their burden of proving by clear and convincing evidence that the claim elements merely involve the "performance of 'well-understood, routine, [and] conventional activities previously known to the industry.'" *Berkheimer*, 881 F.3d at 1367.

2. *Obviousness*

a. *Applicable Legal Principles for Obviousness*

A patent claim is invalid if "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. §103(a). Obviousness is a legal conclusion based on underlying factual determinations, including (1) the scope and content of the

prior art; (2) the differences between the claims and the prior art; (3) the level of ordinary skill in the art; and (4) objective indicia of non-obviousness. See *Purdue Pharma L.P.* v. *Epic Pharma, LLC*, 811 F.3d 1345, 1351 (Fed. Cir. 2016). Prior art under 35 U.S.C. § 102(g) may serve as prior art in an obviousness analysis under § 103. See *Tyco Healthcare Grp. LP* v. *Ethicon Endo-Surgery, Inc.*, 774 F.3d 968, 977 (Fed. Cir. 2014). Section 102(g) states, in relevant part:

> A person shall be entitled to a patent unless . . . before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

35 U.S.C. § 102(g)(2).

The jury was instructed that it "must determine the date of the invention for the alleged prior art" which "can be the date when the invention of the prior art was reduced to practice or when the invention was conceived provided the inventors were diligent in reducing the invention to practice." Final Jury Instructions at 29. The jury was also instructed that:

> Conception is the mental part of an inventive act, i.e., the formation in the mind of the inventor of a definite and permanent idea of the complete and operative invention, enough that one skilled in the art could understand the invention as it is thereafter to be applied in practice. An idea is definite and

> permanent when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue. Where the idea is in constant flux, it is not definite and permanent. A conception is not complete if the subsequent course of experimentation, especially experimental failures, reveals uncertainty that so undermines the specificity of the inventor's idea that it is not yet a definite and permanent reflection of the complete invention as it will be used in practice.

Id. at 29-30; see also *Burroughs Wellcome Co.* v. *Barr Labs., Inc.*, 40 F.3d 1223, 1228 (Fed. Cir. 1994). The jury was further instructed that a "claimed invention is 'reduced to practice' when it has been constructed/used/tested sufficiently to show that it will work for its intended purpose or when the inventor files a patent application." Final Jury Instructions at 30.

Finally, "because obviousness, like any other ground of invalidity, must be established by clear and convincing evidence," the defendant's burden on a JMOL motion is "doubly high: it must show that no reasonable jury could have failed to conclude that [the defendant's] case had been established by clear and convincing evidence." *Boehringer Ingelheim Vetmedica, Inc.* v. *Schering-Plough Corp.*, 320 F.3d 1339, 1353 (Fed. Cir. 2003) (internal citation omitted).

b. *Parties' Contentions*

The jury found that the '755 patent claims were not "invalid as obvious in view of the activities of Dr. Tadatsugu Taniguchi, Dr. Jan Vilček, Dr. David Goeddel, or other prior art." Verdict Form at 3, Q. 9. Defendants assert that there is an insufficient evidentiary basis to uphold the jury's finding that the '755 patent claims are

not invalid for obviousness, and that Defendants "presented largely uncontested evidence" that the claims would have been obvious to a POSA as of June 6, 1980.[30] Defs. Br. at 11.

Defendants identify three "separate and independent" grounds on which they contend the jury should have found the '755 patent claims invalid for obviousness. *Id.* at 10. First, Defendants rely on the scientific work of Tadatsugu Taniguchi, Ph.D. at Harvard University prior to June 6, 1980. Specifically, Defendants rely on Dr. Taniguchi's synthesis of the "117 plasmid" that was designed to produce mature, biologically-active, recombinant human interferon-β in *Escherichia Coli* ("*E. coli*") bacteria cells, and they identify "at least three occasions" before June 6, 1980 on which the 117 plasmid purportedly "produced positive results demonstrating the production of biologically active recombinant JPN-b in *E. coli* in controlled experiments." *Id.* at 11-12. Defendants cite New York University School of Medicine Professor Jan Vilček, M.D., Ph.D.'s trial testimony that his blinded cytopathic effect assay of Dr. Taniguchi's plasma samples provided "ultimate proof" that Dr. Taniguchi had produced biologically-active recombinant interferon-β in *E. coli* in May of 1980. *Id.* at 12.

Second, Defendants rely on the scientific work of David Goeddel, Ph.D. at Genentech, Inc. prior to June 6, 1980. Specifically, Defendants rely on Dr. Goeddel's syn-

---

[30] Dr. Lodish defined a POSA as a person with a "Ph.D. in molecular biology research or comparable work experience or a B.S. in biology, biochemistry, or molecular biology having two or more years in standard laboratory techniques of molecular biology." PDX15-5. Biogen's experts offered opinions at trial based on that definition of a POSA. See 2/15/18 PM Tr. at 49:3-24 (Garcia); 2/20/18 AM Tr. at 26:10-16, 76:20-77:19 (Green).

thesis of the "Trp-69 plasmid" designed to produce mature, biologically-active recombinant interferon-β in *E. coli*, and they identify "at least three occasions" before June 6, 1980 on which Dr. Goeddel purportedly "observed biological activity in experiments testing the product of this plasmid." *Id.* at 14. According to Defendants, the uncontroverted evidence at trial showed that Dr. Taniguchi's and Dr. Goeddel's plasmids could be "scaled up, purified, formulated, and administered using techniques well known by 1980." *Id.* at 15.

Third, Defendants rely on the publication of the DNA sequence for interferon-β and the alleged admissions made by Biogen in an affidavit by '755 patent inventor Dr. Fiers, dated November 19, 2001, which Biogen submitted to the Canadian Patent Office during a conflict proceeding involving Dr. Fiers's Canadian Application No. 374,378 (the "Fiers Affidavit") (STX-0002). In particular, Defendants contend that Biogen admitted that, with the interferon-β DNA sequence in hand, as of June 6, 1980 a POSA would have expected to be able to produce mature, biologically-active, recombinant human interferon-β in *E. coli* that could be used for treating tumors and viruses in humans. *Id.* at 16-17.

In response, Biogen argues that none of the three grounds identified by Defendants merit overturning the verdict, and that Defendants' cited evidence is far from un contested. Biogen contends that there is more than sufficient evidence to support the jury's finding that neither Dr. Taniguchi nor Dr. Goeddel had made the claimed invention prior to June 6, 1980 and, consequently, a POSA would not have found the '755 patent claims obvious in light of the work of these scientists. Biogen Opp. at 20-23. Biogen also asserts that the jury was free to credit the evidence presented by Biogen, including tes-

timony by its experts Michael Green, M.D., Ph.D., a Professor and Chair of the Department of Molecular, Cell, and Cancer Biology at the University of Massachusetts Medical School and Director of the school's Cancer Center (ECF No. 916 at 16; 1/29/18 AM Tr. at 18:15-22), and Christopher Garcia, Ph.D., a Professor of Molecular and Cellular Physiology and a Professor of Structural Biology at Stanford University (ECF No. 916 at 21-22; 2/15/18 PM Tr. at 41:22-25). In Biogen's view, the jury was free to believe Dr. Green's and Dr. Garcia's testimony that a POSA would not have known or reasonably expected that recombinantly-produced interferon-β would be biologically active. Biogen Opp. at 24. Biogen further contends that Defendants walked the jury through the Fiers Affidavit on multiple occasions and in great detail during the trial, and that the jury was free to reject Defendants' obviousness arguments based thereon. *Id.* at 24-25.

c. *Defendants Are Not Entitled to JMOL of Obviousness*

The Court finds that substantial evidence supports the jury's verdict that the '755 patent claims are not invalid for obviousness. The jury was presented with ample fact testimony, expert testimony, and exhibits pertaining to Defendants' obviousness defense. In particular, the jury heard testimony and evidence concerning Dr. Taniguchi's series of experiments carried out prior to June 6, 1980 to test for biological activity of recombinant human interferon-β made in *E. coli*. In making its obviousness determination, the jury was free to weigh the evidence of Dr. Taniguchi's individual experiments that Defendants highlight in their brief against the contrary evidence that certain of Dr. Taniguchi's other experiments yielded false positives, inconclusive results, or results showing no biological activity. See, *e.g.*, Dr. Taniguchi's Laboratory

Notebook (PTX0411) at 6-33, 36-63; 2/5/18 Tr. at 142:2-144:4, 160:5-166:16, 167:1-20 (Taniguchi); 1/24/12 Weissmann Dep. Tr. at 138:2-139:5 (Dr. Taniguchi's mentor testifying that Dr. Taniguchi "did not get expression of biologically-active protein"). For instance, as recorded in Dr. Taniguchi's laboratory notebook page dated June 4 and 5, 1980, one of Dr. Taniguchi's experiments yielded a false positive where the result was marked "should be negative." PTX0411 at 53; see also 2/13/18 AM Tr. At 25:24-28:13 (Lodish) (testifying that false positives can be due to contaminants). In addition, the jury reasonably could have discounted Dr. Vilček's testimony concerning Dr. Taniguchi's allegedly favorable results in light of this contrary evidence, and/or credited Dr. Vilček's other testimony that it was "very possible" that they were still testing for biological activity of recombinant interferon-β after June 6, 1980. 2/6/18 PM Tr. at 51:13-18.

Similarly, the jury was free to weigh the evidence of Dr. Goeddel's three pre-June 6, 1980 experiments that purportedly confirmed biological activity against the contrary evidence that over 100 of Dr. Goeddel's assays, conducted before and after June 6, 1980, were inconclusive or yielded negative results. See 2/20/18 AM Tr. at 64:22-65:7, 65:16-68:17, 69:21-70:4 (Green). For instance, in an experiment on May 20, 1980 upon which Defendants rely and about which Dr. Goeddel had recorded "Looks good!" in his laboratory notebook, Dr. Goeddel detected activity only in a mixed pool of clones that would require further, clone-by-clone testing. See Dr. Goeddel's Laboratory Notebook (STX-0053) at 16; 2/20/18 AM Tr. at 65:12-66:17 (Green) (testifying that Dr. Goeddel's written comment about his preliminary result when read in the context of the laboratory notebook page was merely an "instruction to keep working" rather than a "declaration

of victory"). Dr. Green testified that these results were not conclusive, (2/20/18 AM Tr. at 66:12-24), and in fact, when Dr. Goeddel assayed individual clones eight days later, all of his results were negative, (*id.* at 66:25-67:4; STX-0053 at 20). The jury also saw evidence that in later experiments in May of 1980, Dr. Goeddel noted that his assay was "not a good assay," (STX-0053 at 20), and that the "cells look unhealthy," (PTX0029A at 3375). See 2/20/18 AM Tr. at 67:5-11 (Green); see also *id.* at 71:20-22 (Green) (testifying that there was "no doubt in [his] mind" that Dr. Goeddel did not possess recombinant interferon-β prior to June 6, 1980). Thus, there was sufficient evidence for a reasonable jury to find that Dr. Taniguchi and Dr. Goeddel had not made biologically-active, recombinant interferon-β by June 6, 1980.[31]

---

[31] Defendants assert that, conception aside, prior invention under § 102(g) can occur "if the prior inventor 'reduced to practice' his or her invention before the priority date of the challenged claims." Defs. Reply at 6. Defendants contend that evidence of "a successful experiment" is sufficient to show a prior invention was "reduced to practice" under § 102(g), and that here, the record evidence showed that both Dr. Taniguchi and Dr. Goeddel "actually produced mature human IFNb recombinantly in *E. coli* on multiple occasions" before June 6, 1980. *Id.* at 7. Defendants quote the standard from the doctrine of simultaneous conception and reduction to practice—namely, that "[i]n some instances, an inventor is unable to establish a conception until he has reduced the invention to practice through a successful experiment." *Amgen, Inc.* v. *Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). The jury was instructed, however, that an invention is "reduced to practice" when it has been "constructed/used/tested sufficiently to show that it will work for its intended purpose or when the inventor files a patent application." Final Jury Instructions at 30. Defendants have not sufficiently explained why the jury should have disregarded negative or inconclusive test results and, in any event, the jury was free to disbelieve Defendants' witnesses that any of Dr. Taniguchi's or Dr. Goeddel's preliminary, pre-June 6, 1980 experiments, when viewed in the context of the se-

Defendants contend, however, that the testimony of their experts Dr. Lodish and Dr. Gutterman "provided substantial evidence" that a POSA would have reasonably expected to be able to produce recombinant interferon-β in *E. coli* and that the protein produced would have the biological activity of native interferon-β. Defs. Br. at 16. Contrary to Defendants' assertion, on a Rule 50(b) JMOL motion, the question is not whether substantial evidence supports the moving party's position, but rather whether substantial evidence supports the jury's verdict. See *Power Integrations*, 843 F.3d at 1326 (noting that on a JMOL motion, the moving party "must show that the jury's findings, presumed or express, are not supported by substantial evidence"). Here, the jury heard contrary testimony from Biogen's experts, Dr. Green and Dr. Garcia, that a POSA would not have had a reasonable expectation that recombinantly-produced interferon-β would be biologically active. See 2/20/18 AM Tr. at 75:8-19, 76:9-80:2 (Green); 2/15/18 PM Tr. at 61:23-64:13, 67:10-71:21, 72:24-73:23 (Garcia). For instance, Dr. Green testified that he met the definition of a POSA in 1980 and that, in his opinion, "the notion of going from the DNA sequence, getting an expression vector and having any expectation that it would express biologically active glycosylated protein was well beyond [his] capacity" and "certainly would have taken much more than routine ex-

---

ries of follow-up experiments, constituted "a successful experiment." Viewing the evidence in the light most favorable to Biogen, including testimony by Dr. Taniguchi himself that reproducibility of experiments is important for confirming results, (2/5/18 Tr. at 48:22-49:21), under either Defendants' proposed standard in their motion or the standard set forth in the jury instructions, a reasonable jury could find that Defendants failed to show by clear and convincing evidence that either Dr. Taniguchi or Dr. Goeddel had reduced to practice the claimed invention prior to June 6, 1980.

perimentation." 2/20/18 AM Tr. at 76:20-77:19; see also *id*. at 26:10-16. In addition, Dr. Garcia testified that as of 1980, "no human glycoprotein had ever been expressed in *E. coli* before," (2/15/18 PM Tr. at 58:1-10), and it was an "open question" whether *E. coli's* "primitive simple protein synthesis machinery" would be able to produce interferon-β that folds into the appropriate three-dimensional structure to render it biologically active, (*id*. at 64:4-13).

"[F]aced with competing expert testimony," the jury was free to disbelieve Defendants' experts and credit Biogen's experts. *Intellectual Ventures I LLC* v. *Motorola Mobility LLC*, 870 F.3d 1320, 1327 (Fed. Cir. 2017) (affirming district court's decision denying JMOL where substantial evidence supported jury's verdict that patent claim was not obvious); see also *MobileMedia Ideas LLC* v. *Apple Inc.*, 780 F.3d 1159, 1168 (Fed. Cir. 2015) ("[W]hen there is conflicting testimony at trial, and the evidence overall does not make only one finding on the point reasonable, the jury is permitted to make credibility determinations and believe the witness it considers more trustworthy." (citation omitted)); *Edwards Lifesciences AG* v. *CoreValve, Inc.*, 699 F.3d 1305, 1313 (Fed. Cir. 2012) (noting that when "testimony at trial [is] in direct conflict," the court deciding a JMOL motion "may not weigh the evidence, determine the credibility of witnesses, or substitute its version of the facts for the jury's version" (quoting *Lightning Lube*, 4 F.3d at 1166)). Where, as here, there is "substantial evidence for a reasonable jury finding," it is not this Court's "function to second guess or reevaluate the weight given to that evidence." *MobileMedia*, 780 F.3d at 1168 (citation omitted).

Furthermore, as the Court stated in its decisions denying Defendants' Motion for Summary Judgment of

Invalidity Under 35 U.S.C. § 103 and denying-in-part Biogen's Motion *In Limine* No. 3, the jury was permitted to consider the Fiers Affidavit along with other record evidence in making its obviousness determination. Summ. J. Op. at 9-11; ECF No. 906 at 6-7. The Court concluded that there were genuine issues of material fact "regarding the content of the document and context in which it was submitted that [were] appropriate for a jury's consideration in the first instance." Summ. J. Op. at 9. The Court subsequently declined to preclude any section of the Fiers Affidavit, including those sections that Biogen characterized as legal argument. ECF No. 906 at 6. At trial, the jury heard ample expert testimony and other evidence regarding the Fiers Affidavit and nonetheless rejected Defendants' obviousness defense. In short, the Court denied Defendants' summary judgment motion due to genuine factual disputes, and the jury later resolved those disputes against Defendants. For the reasons set forth in the Court's earlier decisions, the Court declines to hold as a matter of law that the statements in the Fiers Affidavit are binding admissions on Biogen as to the obviousness of the '755 patent claims that warrant overturning the jury's verdict. No new authority has been cited that provides that a district court may substitute an obviousness conclusion drawn by a party or inventor in a foreign proceeding in place of its own analysis. See Summ. J. Op. at 9-10. Moreover, as the Court previously stated, "[t]he obviousness inquiry is undertaken from the perspective of a POSA" and the Federal Circuit "prohibits conducting an obviousness inquiry from the inventor's point of view." *Id.* at 10 n.8 (citing *Arkie Lures, Inc.* v. *Gene Larew Tackle, Inc.*, 119 F.3d 953, 956 (Fed. Cir. 1997)).

Viewing the evidence in the light most favorable to Biogen, the Court finds that substantial evidence supports the jury's finding that the '755 patent claims are not invalid for obviousness. Accordingly, the Court denies Defendants' Rule 50(b) JMOL motion as to obviousness.

3. *Enablement and Written Description*

a. *Applicable Legal Principles for Enablement and Written Description*

The first paragraph of 35 U.S.C. § 112 requires, *inter alia*, that the specification of a patent enable any person skilled in the art to which it pertains to make and use the full scope of the claimed invention. See *Warner-Lambert Co.* v. *Teva Pharms. USA, Inc.*, 418 F.3d 1326, 1336-37 (Fed. Cir. 2005). To invalidate a patent for lack of enablement, "a challenger must show by clear and convincing evidence that a [POSA] would not be able to practice the claimed invention without undue experimentation." *Allergan, Inc.* v. *Sandoz Inc.*, 796 F.3d 1293, 1309 (Fed. Cir. 2015) (internal quotation marks and citation omitted). "Enablement is determined as of the effective filing date of the patent's application." *ALZA Corp.* v. *Andrx Pharms., LLC*, 603 F.3d 935, 940 (Fed. Cir. 2010) (citation omitted). Enablement is a question of law based on underlying factual inquiries. See *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (noting that the analysis of undue experimentation "is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations"). The factors that a court may consider in determining whether a disclosure would require undue experimentation are: "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of

those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Id.*

The written description requirement mandates that "the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharms., Inc.* v. *Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (citation omitted). "[T]he level of detail required to satisfy the written description requirement varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology." *Id.* (citation omitted). Compliance with the written description requirement is a question of fact that must be assessed on a case-by-case basis. See *Allergan*, 796 F.3d at 1308 (citing *Alcon Research*, 745 F.3d at 1190).

Consistent with the Court's rulings denying Defendants' Motion for Summary Judgment of Invalidity Under 35 U.S.C. §112 and Bayer's Motion for Summary Judgment of Invalidity No. 3 (Lack of Written Description), the jury was instructed that "it is the method of treatment that must be [described and enabled], not the proteins to be used or the way they are made." Final Jury Instructions at 36, 38; see also Summ. J. Op. at 14 ("[T]he Court finds that it is not the genus of expression systems that must be enabled and described, it is the method of treatment that must be enabled and described."); *id.* at 30 ("[T]he Court concludes that it is not the recombinant polypeptides themselves that must meet the written description requirement.").

b. *Parties' Contentions*

The jury found that the '755 patent claims were neither invalid for lack of enablement nor for lack of adequate written description. Verdict Form at 4, Qs. 10-11.

Defendants contend that judgment of invalidity for lack of enablement and lack of adequate written description should be entered. Specifically, Defendants assert that the evidence and testimony presented at trial established that the '755 patent fails to enable and describe expression of recombinant interferon-β polypeptides in the full range of "non-human hosts" for administration to human patients. Defs. Br. at 19-21. Defendants also contend that the '755 patent fails to enable and describe the claimed methods of treatment "using the wide scope of the claimed variant polypeptides." *Id.* at 21-22. Lastly, Defendants assert that the '755 patent fails to enable and describe the claimed method of immunomodulation because it does not "teach how to selectively obtain" either upregulation or downregulation of the immune system using recombinant interferon-β, nor does it disclose a use of recombinant interferon-β polypeptides in a method of immunomodulation. *Id.* at 22-23; see also Defs. Reply at 8.

Biogen contends, in response, that sufficient evidence supports the jury's verdict that the claims were neither invalid for lack of enablement nor for lack of adequate written description, and that Defendants merely rehash the arguments raised (and rejected) on summary judgment. Biogen Opp. at 26. Biogen also asserts that Defendants recount their own experts' testimony but omit the contrary evidence on which the jury was entitled to rely. *Id*, at 26-32.

c. *Defendants Are Not Entitled to JMOL of Lack of Enablement or Lack of Adequate Written Description*

The Court finds that substantial evidence supports the jury's verdict that the claims are not invalid for lack of enablement or lack of adequate written description. De-

fendants' motion appears to focus on the scope of the non-human hosts and recombinant polypeptides. As this Court stated in its decision denying Defendants' Motion for Summary Judgment of Invalidity Under 35 U.S.C. § 112, it is not the genus of non-human hosts or recombinant polypeptides that must be enabled and described, it is the method of treatment that must be enabled and described. Summ. J. Op. at 14. Even if Defendants' proposed framework were correct, however, there is ample evidence in the record for a reasonable jury to conclude that the claims are not invalid for either lack of enablement or lack of adequate written description.

i) Non-Human Hosts

With respect to Defendants' contention as to the '755 patent's purported failure to enable expression of recombinant polypeptides in non-human hosts other than E. coli for administration to a patient, Defendants cite Dr. Lodish's trial testimony. They omit, however, the fact that the jury also heard testimony from Biogen's expert, Dr. Green, regarding the availability of non-human hosts other than *E. coli* as of June 6, 1980 as identified in the literature and the '755 patent itself. See 2/20/18 AM Tr. at 26:21-27:8, 106:25-111:13; PTX0001 ('755 patent) at 13:54-64. Additionally, the jury heard evidence that Defendants' own expert, Dr. Lodish, previously testified in a separate lawsuit that "[b]y February 25, 1980 many types of cells had been used as host cells, and workers of ordinary skill in the art had various types of cultured cells that could be used as host cells in transformation experiments." Initial Expert Report of Harvey F. Lodish, Ph.D. dated August 27, 2004 in *In re Columbia University Patent Litigation*, No. 04-MD-01592 (D. Mass.) (PTX1069) at 24; see also 2/20/18 AM Tr. at 109:3-110:18

(Green). Citing various pre-1980 publications, Dr. Lodish had testified in the prior lawsuit that "[s]everal types of human, mouse, and Chinese hamster cell lines, including Chinese Hamster Ovary cells lines, were in routine use." PTX1069 at 24; see also *id.* at 28 (stating that "it was known by February 25, 1980 that one could cause . . . foreign DNA encoding a protein to be expressed in a cultured mammalian cell"). During trial in this case, Dr. Green informed the jury that he was "in complete agreement" with Dr. Lodish's previous statements.[32] 2/20/18 AM Tr. at 110:13-18.

With respect to written description, although Defendants again rely on Dr. Lodish's testimony regarding the '755 patent's purported failure to adequately describe methods of treatment using recombinant polypeptides produced in hosts other than *E. coli*, the jury also heard Dr. Green's testimony that the '755 patent specification

---

[32] In their JMOL motion, Defendants rely on the same Federal Circuit decisions they cited in their summary judgment motion to support their argument that the '755 patent claims cannot be enabled as a matter of law: *Monsanto Co.* v. *Syngenta Seeds, Inc.*, 503 F.3d 1352 (Fed. Cir. 2007), *Plant Genetic Systems, N.V.* v. *DeKalb Genetics Corp.*, 315 F.3d 1335 (Fed. Cir. 2003), *Adang* v. *Fischhoff*, 286 F.3d 1346 (Fed. Cir. 2002), *In re Goodman*, 11 F.3d 1046 (Fed. Cir. 1993), and *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). See Defs. Br. at 19. Defendants contend that in these cases, the Federal Circuit held invalid for lack of enablement claims that were "directed to a genus of host cells that was far narrower than that claimed in the '755 patent" and with later priority dates. *Id.* As this Court stated in its decision denying Defendants' summary judgment motion, these cases "merely reaffirm the fact-specific nature of [the enablement] inquiry." Summ. J. Op. at 16. The jury heard evidence and testimony regarding Defendants' enablement defense and resolved the factual disputes against Defendants. This Court declines to find on a JMOL motion that the '755 patent claims are not enabled as a matter of law based on the cited authority.

expressly describes other host cells that could be used besides *E. coli*, including *Pseudomonas*, *Bacillus subtilis*, *Bacillus stearothermophilus* and other bacilli, yeasts and other fungi, and plant and animal cells. See *id.* at 110:24-111:13; PTX0001 ('755 patent) at 13:54-59. Faced with conflicting expert testimony on these issues, the jury was "permitted to make credibility determinations and believe the witness it consider[ed] more trustworthy." *MobileMedia*, 780 F.3d at 1168.

ii) Recombinant Polypeptides

With respect to Defendants' argument that the '755 patent fails to enable and describe the full range of claimed recombinant interferon-β polypeptides, Biogen's expert, Dr. Garcia, testified that the '755 patent describes the structures likely to be common to the polypeptides meeting the limitations of claim 1, informs the reader "what kinds of changes you can make to the polypeptides while staying within the scope of the patent," including "common optimization" techniques, and "discloses a whole montage of possible tests that one could use to assess the function and the activity of the beta interferon." 2/15/18 PM Tr. at 86:9-89:2. In addition, Dr. Green and Dr. Garcia each described to the jury the various tests for biological activity disclosed in the '755 patent. See 2/20/18 AM Tr. at 30:23-33:5 (Green); 2/15/18 PM Tr. at 88:5-89:2 (Garcia); see also 2/7/18 PM Tr. at 62:15-18 (Gutterman) (agreeing that the '755 patent offers "extensive teaching" about how to test whether any individual polypeptide has the required biological activity). Moreover, Dr. Green opined that the patent describes and enables the therapeutic use of recombinant interferon-βeta-like proteins. 2/20/18 AM Tr. at 23:8-12. Again, while Defendants cite expert testimony favorable to their § 112

invalidity defenses, as discussed above with respect to the jury's obviousness determination, faced with competing expert testimony, the jury was free to disbelieve Defendants' experts and credit Biogen's experts. See *Intellectual Ventures*, 870 F.3d at 1327; *MobileMedia*, 780 F.3d at 1168; *Edwards Lifesciences*, 699 F.3d at 1313.

iii) Immunomodulation

Sufficient evidence also supports the jury's finding that the '755 patent enables and describes the use of recombinant interferon-β polypeptides for immunomodulation. The Court provided the jury with its definition of the term "immunomodulation" as "regulation of the immune system by immunopotentiation (up-regulation) or immunosuppression (down-regulation)." Final Jury Instructions at 17. The '755 patent discloses that interferon-β may "play a role in regulation of the immune response" and "can be both immunopotentiating and immunosuppressive in vivo and in vitro." PTX0001 ('755 patent) at 3:33-36. The jury was free to reject Dr. Gutterman's testimony that "a clinician would need to know how to 'selectively obtain' upregulation or downregulation of the immune system in order to use IFN-β in a therapeutically effective manner." Defs. Br. at 22 (citing 2/7/18 AM Tr. at 75:13-19 (Gutterman)). Contrary to Defendants' assertion, there is no requirement that immunomodulation means exclusively up-regulation or exclusively down-regulation, and the jury was not asked to determine whether, in treating MS, interferon-β acts by only up-regulation or only down-regulation. Moreover, the jury heard expert testimony and was presented with evidence, including Pfizer's and Serono's own internal presentations and statements to the FDA, showing that interferon-β upregulates some parts of the immune sys-

tem and downregulates others in treating MS. See, *e.g.*, 1/29/18 PM Tr. at 22:17-19, 23:17-29:11, 32:14-33:24, 38:19-24, 40:9-42:2 (Kinkel); PTX0059 (Rebif® BLA) at 163; PTX0061 (Rebif® BLA) at 19-20; PTX0227 (Serono presentation) at 1, 26-29; PTX0659 (Pfizer presentation) at 14, 87; PTX0056 (Betaseron® Product License Application) at 77-78, 922. The jury was free to believe this evidence and testimony in reaching its verdict on Defendants' § 112 defenses. Finally, a reasonable jury could have also credited the evidence that the issue of whether the patent sufficiently describes and enables the full scope of the claims was before the PTO when it issued the patent. See, *e.g.*, 2/15/18 PM Tr. at 99:2-11 (Garcia); 2/20/18 AM Tr. at 111:9-13 (Green); 2/7/18 AM Tr. at 94:24-95:24 (Gutterman); see also *Microsoft*, 564 U.S. at 111, 131 S.Ct. 2238.

Viewing the evidence in the light most favorable to Biogen, the Court finds that substantial evidence supports the jury's finding that the '755 patent claims are not invalid for lack of enablement or lack of adequate written description. Accordingly, the Court denies Defendants' Rule 50(b) JMOL motion as to enablement and written description.

4. *Contributory Infringement By Pfizer*

   a. *Applicable Legal Principles for Contributory Infringement*

Section 271(c) of the Patent Act deems a "contributory infringer" one who "offers to sell or sells" within the United States a "component of a patented machine, manufacture, combination or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article

or commodity of commerce suitable for substantial noninfringing use." 35 U.S.C. §271(c). The patentee bears the burden of proving contributory infringement by a preponderance of the evidence. See *Octane Fitness*, 134 S.Ct. at 1758; *Seal-Flex*, 172 F.3d at 842.

The Federal Circuit has explained that the "ordinary meaning of a sale" under Section 271 "includes the concept of a transfer of title or property" and may be determined by "the agreement by which such a transfer takes place." *Halo Elecs., Inc.* v. *Pulse Elecs., Inc.*, 769 F.3d 1371, 1379 (Fed. Cir. 2014) (citations omitted), vacated and remanded on other grounds, —— U.S. ——, 136 S.Ct. 1923, 195 L.Ed.2d 278 (2016); *NTP, Inc.* v. *Research In Motion, Ltd.*, 418 F.3d 1282, 1319 (Fed. Cir. 2005), abrogated on other grounds, *Zoltek Corp.* v. *United States*, 672 F.3d 1309 (Fed. Cir. 2012).

In addition, an "offer to sell is a distinct act of infringement separate from an actual sale" and "differs from a sale in that an offer to sell need not be accepted to constitute an act of infringement." *Transocean Offshore Deepwater Drilling, Inc.* v. *Maersk Contractors USA, Inc.*, 617 F.3d 1296, 1308 (Fed. Cir. 2010) (citing *MEMC Elec. Materials, Inc.* v. *Mitsubishi Materials Silicon Corp.*, 420 F.3d 1369, 1376 (Fed. Cir. 2005)). An offer to sell is analyzed "using traditional contract principles." *Id.* (citing *Rotec Indus., Inc.* v. *Mitsubishi Corp.*, 215 F.3d 1246 (Fed. Cir. 2000)). An alleged infringer must "communicate[ ] a 'manifestation of willingness to enter into a bargain, so made as to justify another person in understanding that his assent to that bargain is invited and will conclude it.'" *MEMC*, 420 F.3d at 1376 (quoting *Rotec*, 215 F.3d at 1257). "The underlying purpose of holding someone who offers to sell liable for infringement is to prevent 'generating interest in a potential infringing

product to the commercial detriment of the rightful patentee.'" *Transocean*, 617 F.3d at 1309 (quoting *3D Sys., Inc.* v. *Aarotech Labs., Inc.*, 160 F.3d 1373, 1379 (Fed. Cir. 1998)).

b. *Parties' Contentions*

The jury found that Pfizer "has contributed to the direct infringement of the asserted claims of the '755 patent by healthcare professionals and/or patients by selling or offering to sell Rebif." Verdict Form at 3, Q. 8. Defendants contend that there is no legally sufficient evidentiary basis on which the jury could have found that Pfizer has contributorily infringed the asserted claims of the '755 patent under 35 U.S.C §271(c).[33] According to Defendants, while Pfizer has previously co-promoted Rebif® with Serono, Pfizer did not and does not sell, offer to sell, or import Rebif® into the United States.[34] Defs. Br. at 23. Defendants assert that the jury heard evidence that while Pfizer has the right to promote (or detail) Rebif®, it does not have the right to sell Rebif®, as reflected in Serono and Pfizer's collaboration agreement dated

---

[33] Defendants do not challenge the jury's finding that Serono has contributed to the infringement of the asserted claims. See Verdict Form at 3, Q. 7.

[34] Defendants' challenge to the jury's finding of contributory infringement against Pfizer relates solely to the issue of whether Pfizer "sold or offered to sell Rebif in the United States during the time the '755 patent was in force, from September 2009 to the present." Final Jury Instructions at 24. Defendants do not challenge the jury's findings with respect to the other elements of contributory infringement—namely, that "healthcare professionals and/or multiple sclerosis patients using Rebif directly infringe the '755 patent in the United States," that "Rebif has no substantial, non-infringing use," or that Pfizer "was aware of the '755 patent and knew that Rebif was being used by healthcare professionals and/or patients in a manner that infringes a claim of the '755 patent." *Id.*

July 10, 2002 (STX-946). *Id.* at 23-24. The collaboration agreement provides that Serono "grants to Pfizer the exclusive right, together with SERONO, to promote and Detail (but not to sell) the Product in the Territory in the Field." STX-946 at 10. Defendants also cite deposition testimony of Pfizer's corporate representatives in arguing that "Pfizer indisputably has no title or property interest in Rebif to transfer." Defs. Br. at 23-24. Moreover, in Defendants' view, "Pfizer cannot offer to sell what it does not have the right or ability to sell." *Id.* at 24.

Biogen contends, in opposition, that sufficient evidence supports the jury's determination that Pfizer sells Rebif®, offers to sell Rebif®, or both. Biogen Opp. at 32. With respect to Pfizer purportedly selling Rebif®, Biogen asserts that Defendants' brief omits the collaboration agreement's provision requiring Serono and Pfizer to "work diligently and use reasonable efforts to promote the sale of" Rebif® in the United States. *Id.* at 33-34; STX-946 at 22, § 5.1. Biogen also contends that the jury heard evidence regarding Pfizer's efforts to support the sale and marketing of Rebif® in exchange for a share of the net sales of Rebif®, and that Serono and Pfizer do not know whether any given sale of Rebif® is due to Serono's or Pfizer's detailing efforts. Biogen Opp. at 34-35. Moreover, Biogen asserts, in support of its argument that Pfizer offers to sell Rebif®, that Pfizer's sales representatives visit thousands of doctors and nurses each year to "encourage them to prescribe Rebif®," and that Defendants' argument that Pfizer cannot "offer to sell" Rebif® because Pfizer cannot "sell" Rebif® "blinks reality." *Id.* at 37-38.

c. *Defendants Are Not Entitled to JMOL of No Contributory Infringement By Pfizer*

The Court finds that substantial evidence supports the jury's verdict that Pfizer is liable for contributory infringement. In particular, substantial evidence supports a finding that Pfizer at least "offers to sell" Rebif® within the United States.

Defendants contend that Pfizer cannot, as a matter of law, "offer to sell" Rebif® within the meaning of §271(c) because Pfizer merely details Rebif® and Serono, not Pfizer, is the company that manufactures Rebif® and ultimately transfers title to the drug. See, *e.g.*, Defs. Br. at 24 ("Pfizer cannot offer to sell what it does not have the right or ability to sell."); *id.* at 24 n.5 (Pfizer "could not enter into any bargain regarding the sale of Rebif"). Defendants do not appear to cite authority that supports such a proposition. Nor have Defendants persuaded this Court to hold as a matter of law that a contractual provision granting a company the right to promote (or detail) "but not to sell" a product singularly shields that company from liability for "offering to sell" a product under §271. Rather, determining whether there has been an "offer to sell" requires applying traditional contract law principles to the particular facts of the case, taking into account the circumstances in which such offers are made. In this case, the jury heard testimony regarding the "structure and realities of the heavily regulated pharmaceutical industry." *Christopher* v. *SmithKline Beecham Corp.*, 635 F.3d 383, 396 (9th Cir. 2011), aff'd, 567 U.S. 142, 132 S.Ct. 2156, 183 L.Ed.2d 153 (2012). Since "federal law prohibits pharmaceutical manufacturers from directly selling prescription medications to patients," *id.*, companies such as Serono and Pfizer promote pharmaceutical drug products to physicians through a process

called "detailing," whereby their sales representatives "provide information to physicians about the company's products in hopes of persuading them to write prescriptions for the products in appropriate cases," *Christopher*, 567 U.S. at 150, 132 S.Ct. 2156 (citation omitted).[35] Although not a patent case, the Ninth Circuit in *Christopher* described the process in detail and defined a "sale" in this industry as the "exchange of nonbinding commitments between the [sales representative] and physician at the end of a successful call." 635 F.3d at 396 ("Through such commitments, the manufacturer will provide an effective product and the doctor will appropriately prescribe; for all practical purposes, this is a sale.").

The evidence presented at trial, from which the Court draws all reasonable inferences in favor of Biogen, demonstrates that Pfizer's conduct at least constitutes an "offer to sell" Rebif® within the meaning of § 271(c). For instance, Defendants' collaboration agreement explicitly requires that both Serono and Pfizer "work diligently and use reasonable efforts to promote the sale of" Rebif® in the United States. STX-946 at 22, § 5.1. The agreement also requires Serono to make "commission payments" to Pfizer based on a percentage of the net sales of Rebif® and requires Pfizer to make sales of Rebif® "a factor in the determination of the incentive compensation for its Sales Representatives." *Id.* §§ 5.2, 7.2.

In addition, Pfizer's sales team, comprised of about 75,000 sales representatives, visits healthcare professionals across the country to persuade them to prescribe Rebif® to their patients. 1/31/13 Mehl Dep. Tr. at 21:13-22:15, 23:7-15, 31:3-6. Indeed, various Serono and Pfizer

---

[35] Pfizer's corporate representative provided a similar definition of "detail." 1/25/13 Gans Dep Tr. at 37:20-38:14.

representatives testified regarding Pfizer's efforts to support the sale and marketing of Rebif® in exchange for a share of the net sales of Rebif®. See, *e.g.*, 1/25/13 Gans Dep. Tr. at 23:8-24:3 (stating that both Serono and Pfizer are "involved in the . . . actual sale of—or the promotion of Rebif to physicians at the . . . sales level or the field level"); *id.* at 34:6-20 (Pfizer gets "a share of the net sales" of Rebif®); 1/11/13 Huycke Dep. Tr. at 65:8-24 (explaining that Serono and Pfizer each deploys a salesforce across the United States and have a "shared responsibility" over the sale of Rebif®); 2/13/13 Moore Dep. Tr. at 21:17-22:8, 22:10-21 (stating that "detailing is intended to lead to greater prescription, which would lead to sales"); 1/31/13 Mehl Dep. Tr. at 21:13-22:15, 23:7-15, 31:3-6 (explaining that there is a "sales team on both sides" and agreeing that Pfizer "sell[s] Rebif" by helping "promote the product through a contract with" Serono). Based on this evidence and testimony, a reasonable jury could have determined that Pfizer could, in fact, "enter into a bargain" regarding the sale of Rebif®, and that a pharmacy would thereafter fill a prescription for Rebif® from a physician visited by a Pfizer sale representative. See 1/11/13 Huycke Dep. Tr. at 74:21-75:13 (explaining that after a successful detail, typically "the prescription will be written in the form of an SRF, which can, one means, be faxed to the MS Lifelines or the prescription could be given to a specialty pharmacy, and that will trigger the reimbursement, the verification and eventually the product shipment"). Indeed, the evidence showed that neither Serono nor Pfizer knows whether any given sale of Rebif® is due to Serono's or Pfizer's sales team's detailing efforts. See 1/25/13 Gans Dep. Tr. at 36:21-24 (explaining that there is "no mechanism" to track sales due to either company's marketing efforts); *id.* at 25:5-16 (stating that "[m]ost territories are shared by Pfizer and

Serono" sales representatives and an individual doctor may get called on by a sales representative from both companies). That Serono is the source of Rebif® and ultimately transfers title to Rebif® does not preclude the jury's having found that Pfizer "offers to sell" Rebif®.[36] Sufficient evidence supports such a finding, and Defendants have not cited authority that warrants disrupting that finding.

Viewing the evidence in the light most favorable to Biogen, a reasonable jury could have found by a preponderance of the evidence that Pfizer is liable for contributory infringement. Accordingly, the Court denies Defendants' Rule 50(b) JMOL motion as to contributory infringement by Pfizer.

---

[36] Defendants cite *Milo & Gabby, LLC* v. *Amazon.com*, 144 F.Supp.3d 1251, 1252-53 (W.D. Wash. 2015), aff'd sub nom. *Milo & Gabby LLC* v. *Amazon.com, Inc.*, 693 F. App'x 879 (Fed. Cir. 2017), to support their argument that Pfizer "could not enter into any bargain regarding the sale of Rebif" and for the proposition that "[a]n offer is the manifestation of willingness to enter into a bargain, so made as to justify another person in understanding that his assent to that bargain is invited and will conclude it." Defs. Br. at 24 n.5. In that case, the district court adopted the jury's advisory verdict that online retailer Amazon did not "offer to sell" the accused products by allowing non-party "sellers" to list such products on Amazon's website. *Amazon.com*, 144 F.Supp.3d at 1252. The court's ruling was based on a review of the record and the jury's specific factual findings that Amazon did not communicate through its website a description or price of the products or that it was willing to enter into a bargain to sell the products. *Id.* Here, based on a review of the record evidence and considering the particular practices within the pharmaceutical industry, it would not have been unreasonable for the jury to have found that Pfizer's sales representatives, in their face-to-face meetings with healthcare providers, "manifest[ed] [a] willingness to enter into a bargain" regarding the prescription and sale of Rebif®.

5. *Lost Profits Damages*

a. *Legal Principles for Lost Profits Damages*

The legal principles for lost profits damages are set forth in the Court's discussion in Section III.A.4 above regarding Biogen's JMOL motion as to subsidiary damages issues.

b. *Parties' Contentions*

As discussed above, the jury did not reach the damages questions on the Verdict Form, having concluded that the '755 patent claims are invalid as anticipated over the prior-art uses of native interferon-β. Defendants seek a judgment that Serono's right to license the '755 patent forecloses Biogen's lost profits claim because "no reasonable jury could conclude that Serono would ever be off the market." Defs. Br. at 25. According to Defendants, Biogen's own witnesses testified that a market without Rebif® is "inconceivable" and that the evidence showed that Serono would have exercised its unilateral right to sell Rebif® under license rather than leave the market. *Id.* Defendants also reiterate the arguments in their *Daubert* motion to preclude Biogen's damages expert Kevin Murphy, Ph.D.'s testimony, arguing that his damages analysis improperly disregarded Serono's non-infringing alternative action and suggested that patent damages are intended to punish Serono rather than compensate Biogen. *Id.* at 26.

In response, Biogen contends that Defendants merely restate their arguments that the Court rejected in denying their summary judgment motion, in denying their *Daubert* motion against Dr. Murphy, and during the crafting of the jury instructions. Biogen Opp. at 38. Biogen also argues that contrary to Defendants' assertion, there was substantial evidence that Serono believed that the Nonsuit and Option Agreement did not even apply to

sales of Rebif®, and that this was the same evidence the Court considered when it denied Defendants' summary judgment motion. *Id.* at 39-40 (citing 7/22/16 Newland Dep. Tr. at 18:18-19:22, 42:20-44:4, 60:21-61:4, 61:7-61:24, 70:17-72:20, 72:22-24; 1/31/18 Tr. at 53:5-17 (De Luca); 3/22/16 Brudnick Dep. Tr. at 14:17-15:10).

c. *Defendants Are Not Entitled to JMOL as to Lost Profits Damages*

As discussed above, the Court orders a new trial on all damages issues, including the issue of whether licensed Rebif® constitutes a non-infringing alternative. Again, the Court declined to conclude on summary judgment that the Nonsuit and Option Agreement precludes Biogen's claim of lost profits as a matter of law. ECF No. 884. In particular, the Court determined that Serono's motion raised genuine issues of material fact that were appropriate for a jury's consideration. *Id.* at 10-12. In instructing the jury on the law of damages, the Court stated that the jury "must take into account, where relevant, alternative actions that Serono would have undertaken had it not infringed." Final Jury Instructions at 43. During the trial both sides presented expert testimony in support of their positions on this issue, and the jury did not reach the question of damages. Defendants largely reiterate the same case law they cited in their summary judgment motion as to Biogen's claim of lost profits, and have not cited new authority that would compel this Court to rule as a matter of law that the Nonsuit and Option Agreement forecloses Biogen's lost profits claim. Accordingly, the Court denies Defendants' Rule 50(b) JMOL motion as to lost profits damages.

IV. CONCLUSION

For the reasons discussed above, Biogen's JMOL motions with respect to anticipation, induced infringement

against Pfizer and Serono, and certain non-litigated defenses are hereby **GRANTED**. The Court also conditionally orders a new trial on anticipation and induced infringement against Pfizer and Serono pursuant to Rule 50(c), and orders a new trial on all damages issues pursuant to Rule 59. Biogen's remaining JMOL motions and each of Defendants' JMOL motions are hereby **DENIED**. An appropriate Order will be entered.

Date: September 7, 2018

s/Hon. Claire C. Cecchi
Hon. Claire C. Cecchi
United States District Judge

APPENDIX F

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

NO. 2019-1133

BIOGEN MA INC.,

Plaintiff-Appellee,

v.

EMD SERONO, INC.,
PFIZER INC.,

Defendants-Appellants,

BAYER HEALTHCARE PHARMACEUTICALS INC.,
NOVARTIS PHARMACEUTICALS CORPORATION

Defendants.

Appeal from the United States District Court for the District of New Jersey in No. 2:10-cv-02734-CCC-MF, District Judge Claire C. Cecchi.

ON PETITION FOR PANEL REHEARING
AND REHEARING EN BANC

December 18, 2020

Before PROST, *Chief Judge*, NEWMAN, LOURIE, LINN[*], DYK, MOORE, O'MALLEY, REYNA, WALLACH, TARANTO, CHEN, HUGHES, and STOLL, *Circuit Judges*.

PER CURIAM.

ORDER

Appellee Biogen MA Inc. filed a combined petition for panel rehearing and rehearing en banc. A response to the petition was invited by the court and filed by Appellants EMD Serono, Inc. and Pfizer Inc. The petition was referred to the panel that heard the appeal, and thereafter the petition for rehearing en banc was referred to the circuit judges who are in regular active service.

Upon consideration thereof,

IT IS ORDERED THAT:

The petition for panel rehearing is denied.

The petition for rehearing en banc is denied.

The mandate of the court will issue on December 28, 2020.

FOR THE COURT

December 18, 2020
Date

/s/ Peter R. Marksteiner
Peter R. Marksteiner
Clerk of Court

[*] Circuit Judge Linn participated only in the decision on the petition for panel rehearing.

APPENDIX G

RELEVANT STATUTORY PROVISION

1. The 2006 version of Title 35 of the U.S. Code provides in relevant part as follows:

§ 102. Conditions for patentability; novelty and loss of right to patent

A person shall be entitled to a patent unless—

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or

(b) the invention was patented or described in a printed publication in this or a foreign country or in. public use or on sale in this country, more than one year prior to the date of the application for patent in the United States, or

(c) he has abandoned the invention, or

(d) the invention was first patented or caused to be patented, or was the subject of an inventor's certificate, by the applicant or his legal representatives or assigns in a foreign country prior to the date of the application for patent in this country on an application for patent or inventor's certificate filed more than twelve months before the filing of the application in the United States, or

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the

international application designated the United States and was published under Article 21(2) of such treaty in the English language;[1] or

(f) he did not himself invent the subject matter sought to be patented, or

(g)(1) during the course of an interference conducted under section 135 or section 291, another inventor involved therein establishes, to the extent permitted in section 104, that before such person's invention thereof the invention was made by such other inventor and not abandoned, suppressed, or concealed, or (2) before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

---

[1] So in original. The semicolon probably should be a comma.