IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

CHROMADEX, INC. and TRUSTEES OF DARTMOUTH COLLEGE,

Plaintiffs,

v.

ELYSIUM HEALTH, INC.,

Defendant.

Civil Action No. 18-1434-CFC

[redacted]

PLAINTIFFS' RESPONSE TO ELYSIUM'S MOTION FOR SUMMARY JUDGMENT (NO. 3) OF INVALIDITY UNDER 35 U.S.C. § 112 (D.I. 197)

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TABLE OF ABBREVIATIONS

Abbreviation	Description
The Dartmouth Patents	U.S. Patent Nos. 8,383,086 and 8,197,807
The '807 Patent	U.S. Patent No. 8,197,807
The '086 Patent	U.S. Patent No. 8,383,086
ChromaDex	Plaintiff ChromaDex, Inc.
Dartmouth	Plaintiff Trustees of Dartmouth College
Plaintiffs	collectively, Plaintiffs ChromaDex, Inc. and Trustees of Dartmouth College
Elysium	Defendant Elysium Health, Inc.
NR	nicotinamide riboside
Ex.	Exhibit of Declaration of Adam W. Poff in Support of Plaintiffs' Response to Elysium's Motion for Summary Judgment (No. 3) of Invalidity under 35 U.S.C. § 112
D.I. 197	Elysium's Opening Brief in Support of Motion for Summary Judgment (No. 3) of Invalidity Under 35 U.S.C. § 112, D.I. 197 (Apr. 27, 2021)
SF3	Elysium Health's Statement of Facts in Support of its Motion for Summary Judgment (No. 3) of Invalidity under 35 U.S.C. § 112
XSF3	Plaintiffs' Counter Statement of Facts in Opposition to Elysium's Motion for Summary Judgment (No. 3) of Invalidity under 35 U.S.C. § 112

Elysium's motion argues that the Asserted Claims lack enablement and written description support because, it alleges: (1) the claim term "nicotinamide riboside" has nearly infinite scope and (2) determining the compositions of "nicotinamide riboside" that increase NAD^+ biosynthesis or improve the health/welfare of an animal would require "extensive, unpredictable, brute force testing." Plaintiffs and their experts disagree. As Plaintiffs' experts demonstrate, "nicotinamide riboside" as used in the Dartmouth Patents, has a limited scope, and any testing required to practice the claimed inventions would be routine.

These are genuine disputes of material fact. Elysium's motion for summary judgment, however, baldly attempts to conceal these disputes. At every turn, Elysium mischaracterizes the factual bases of their motion as "undisputed." Indeed, the factual underpinnings of Elysium's motion are not only disputed, they are demonstrably wrong. Elysium's motion should thus be denied.

BACKGROUND

Elysium asserts that "Plaintiffs do not challenge the underlying facts." D.I. 197, 1. This is false.

First, Plaintiffs and their experts do not accept Elysium's purportedly "undisputed" assertion that "there are 'more than thousands' of derivatives of NR." D.I. 197, 2; XSF-16. Elysium tries to support this assertion with testimony from Plaintiffs' expert, but Dr. Larsen never agreed that there are "at least thousands of

ester derivatives of NR." Rather, as Dr. Larsen explained in his report, a POSA "would thus recognize salts and/or esters of nicotinamide riboside as a comprehensible class of derivatives having nicotinamide riboside as their active moiety." Ex. 4, ¶ 32. A POSA would reach this conclusion based on the specification's teachings concerning derivatives of NR, *id*., ¶ 26, a POSA's knowledge and experience, *id.*, ¶¶ 27-29, and the specification's description of the prior examples of ester derivatives, *id*., ¶ 30.

Notably, the portion of Dr. Larsen's deposition transcript Elysium cites in D.I. 197 and SF3-03—*i.e.*, Ex. 3, 38-39—has nothing to do with ester derivatives of NR. The questions and answers cited by Elysium relate instead to the number of esters in general, not the patent's meaning of the term derivative. *E.g.*, Ex. 3, 39:8-10, 41:7-11. Indeed, immediately following the testimony cited by Elysium, Dr. Larsen expressly clarified: "The patent refers to ester derivatives in the context of the patent … . So going down the list of all the possible esters I don't see why -- that's way outside the context of this patent." *Id*., 40:15-41:6. Elysium mischaracterizes Dr. Larsen's testimony as about ester derivatives when it was really about general chemistry.

Second, Plaintiffs and their experts reject Elysium's purportedly "undisputed" assertion that "identifying the compositions comprising NR derivatives that would increase NAD+ biosynthesis or improve health/welfare of any animal would require

extensive, unpredictable, brute force testing." D.I. 197, 3; XSF3-17; XSF3-18. Plaintiffs' experts have consistently maintained the opposite—that the amount of testing required to practice the claimed inventions would be "routine." *See, e.g.*, Ex. 5, ¶¶ 1021, 1032-33; Ex. 4, ¶¶ 25-27.

Elysium points to testimony from the inventor of the Asserted Patents (SF3-05) and Plaintiffs' experts (SF3-06, SF3-07), as alleged support for the proposition that "extensive, unpredictable, brute force testing," *see* D.I. 197, 3-4, but the cited testimony merely establishes that routine testing would be required for certain derivatives. It does not indicate a lack of genuine dispute. To the contrary, Plaintiffs' experts' testimony directly contradicts Elysium's assertion. *E.g.*, Ex. 3, 93:11-17 ("[S]omeone who is skilled in the art would understand what's required to do to test that and this would be routine for someone to look into."); XSF3-17; XSF3-18.

ARGUMENT

I. Elysium, not Plaintiffs, disregards the Court's construction.

The Court construed "nicotinamide riboside" as "nicotinamide riboside or a derivative (e.g., L-valine or L-phenylalanine esters) of nicotinamide riboside." The experts dispute application of this claim construction, with Elysium's expert notably ignoring the exemplary derivatives expressly set forth in the construction, as well as the patent specification's description of their function. This dispute should preclude

summary judgment. *See, e.g.*, *Baxalta Inc. v. Bayer Healthcare LLC*, No. 17-1316-RGA, 2021 WL 184404, at *15 (D. Del. Jan 19, 2021).

The specification describes the derivatives that are within the scope of the patent:

> [T]he nicotinamide riboside can be a derivative (e.g., L-valine or L-phenylalanine esters) of nicotinamide riboside. For example, an L-valyl (valine) ester on the 5' O of acyclovir (valacyclovir) improved the pharmacokinetic properties of the drug by promoting transport and allowing cellular delivery of the nucleoside after hydrolysis by an abundant butyryl esterase.… Accordingly, ***the present invention also encompasses derivatives of nicotinamide riboside, in particular L-valine or L-phenylalanine esters of nicotinamide riboside, which are contemplated as having improved pharmacokinetic properties (e.g., transport and delivery)***.

Ex. 1, '807 Patent, 28:58-29:10 (emphasis added, citations omitted); Ex. 2, '086 Patent, 28:21-35 (same).

Drs. Sobol and Larsen opined that a POSA reading the patent specification would understand a "derivative (e.g., L-valine or L-phenylalanine esters)" to have shared characteristics, such as being a salt or ester of similar structure. *E.g.*, Ex. 4, ¶ 26; Ex. 5, ¶¶ 1002-03; XSF3-16. Strikingly, Dr. Adams, in the declaration he submitted in support of Elysium's claim construction, took a similar approach, representing to the Court that "[t]wo common ways of derivatizing a compound for oral administration as of 2004 were creating salts and ester forms of the compound" and that "[a] person of ordinary skill in the art, reading the claims in view of the

specification, would understand the 'nicotinamide riboside' in the claims to include nicotinamide riboside … as well as derivatives of nicotinamide riboside (including at least both salts and esters)." Ex. 6, ¶¶ 13, 18. Dr. Adams did not suggest during claim construction that the claims encompass "derivatives" of NR beyond salts and esters like the L-valine and L-phenylalanine ones. *See* Ex. 7, 256:19-259:22 (conceding specification describes certain salt and ester derivatives having common structural and functional properties); Ex. 1, '807 Patent, 29:4-8. Drs. Sobol and Larsen's opinions concerning the compounds constituting a "derivative (e.g., L-valine or L-phenylalanine esters)" of NR are fully consistent with the claim construction record. XSF3-16.

By contrast, it is Elysium that now abandons the Court's claim construction and the existing record. Dr. Adams simply ignores the portion of the claim construction referring to the L-valine or L-phenylalanine esters and makes no effort to apply a POSA's understanding of the patent specification's description of the NR derivatives. *See* Ex. 7, 259:14-260:3, 265:21-266:2. He maintains that a "derivative" is any compound that contains the NR structure substituted with any "arbitrary substituent" at any position. *See, e.g.*, Ex. 8, ¶ 784; Ex. 9, ¶ 279.[1]

[1] Indeed, Dr. Adams does not even stop there, but opines further that any molecule that can be made starting with NR (or similar compounds) would be a "derivative" of NR within the scope of the claims. Ex. 7, 261:11-262:4.

Drs. Larsen and Sobol disagree with Dr. Adams for multiple reasons. For example, Dr. Adams' interpretation treats compounds such as NMN and NAD^+ as "nicotinamide riboside" under the Dartmouth Patents, even though the patents expressly distinguish those compounds from NR. Ex. 5, ¶ 1001 (citing '807 Patent (Ex. 1), 8:9-11). Further illustrating his error, Dr. Adams' broad and open-ended view of NR "derivatives" leads him to the impossible and contradictory conclusion that NMN is both (1) a "derivative" of NR within the scope of the claims, Ex. 9, ¶ 313, and also (2) a non-infringing alternative to the claimed compositions comprising isolated NR, Ex. 10, ¶¶ 79, 83. *See* Ex. 7, 184:21-186:21. Moreover, many compounds that Dr. Adams identified as derivatives of NR would not deliver NR upon oral administration, thus contradicting the patent's teachings about the claimed derivatives. Ex. 4, ¶¶ 36-38; XSF3-15.

Elysium argues that the patent specification's reference to "cellulose, and its derivatives, such as sodium carboxymethylcellulose, ethyl cellulose and cellulose acetate" contradicts Plaintiffs' experts. D.I. 197, 6 (citing SF3-13). That is incorrect. The cited passage makes clear that, when the patent describes the use of derivatives, it exemplifies the type of derivatives to be used. That the type of cellulose derivatives useful as excipients would be different than the type of NR derivatives useful for delivering NR to the body is unsurprising, and a POSA would not understand the

exemplified cellulose derivatives to inform the scope of useful NR derivatives. XSF3-12.

Dr. Adams' own testimony presents internal material factual disputes on the subject of "derivative (e.g., L-valine or L-phenylalanine esters) of nicotinamide riboside." And Elysium is wrong when it alleges that Drs. Larsen and Sobol "refus[ed] to follow this Court's construction" of "nicotinamide riboside." D.I. 197, 5. Plaintiffs' experts simply disagreed with Elysium's untethered interpretation of the term "derivative." XSF3-15; XSF3-16. Because there is a genuine dispute of material facts related to what a POSA would understand a derivative of NR to encompass, Elysium's motion for summary judgment should be denied.

II. The claims of the Dartmouth Patents are enabled.

Elysium's enablement theory hinges on its assertions that there are at least thousands of derivatives of NR, *see, e.g.*, D.I. 197, 10 n.5, and that "undue experimentation would be required to know which compositions comprising NR derivatives meet the claims," *id*., 7. Plaintiffs have presented genuine disputes regarding both factual assertions, as described above, and Elysium's motion should be denied as a result. *See Vectura Ltd. v. GlaxoSmithKline LLC*, No. 16-638-RGA, 2019 WL 1244942, at *4 (D. Del. Mar. 18, 2019); *Evonik Degussa GmbH v. Materia Inc.*, No. 09-cv-636, 2016 WL 337378, at *8 (D. Del. Jan. 26, 2016).

When the proper meaning and scope of derivative is used, a POSA would understand that derivatives of NR represent a comprehensible and limited class of salts and/or esters commonly used to deliver active compounds, such as NR or acyclovir. *See* above; XSF3-15; XSF3-16. In addition, a POSA would require no more than routine experimentation to practice the full scope of the claims. XSF3-17. Strikingly, even Dr. Adams agreed that derivatizing a compound was common as of 2004, Ex. 6, ¶ 13, and there is no dispute that making and using salts of NR would be straightforward. XSF3-18.

The cases Elysium cites in support of its argument, *Idenix* and *Wyeth*, relate to the experimentation required to determine whether tens of thousands of different active compounds are effective at inhibiting a particular enzyme. *See Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149, 1157 (Fed. Cir. 2019)*; Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1385 (Fed. Cir. 2013). The present case is different because it relates to a single active compound—NR. Unlike the compounds claimed in *Idenix* and *Wyeth*, the derivatives at issue here are those that deliver NR, not thousands of unrelated structures that may or may not deliver NR and may or may not increase NAD^+ biosynthesis or improve the health/welfare of an animal. Moreover, it was a common practice to derivatize active compounds by known methods to improve delivery, *see* Ex. 6, ¶ 13; Ex. 1, '807 Patent, 28:65-29:8, and it is undisputed that NR can be effective at increasing NAD^+ biosynthesis.

Elysium also suggests that the Asserted Claims include broad functional limitations that would "pose high hurdles" to enablement. D.I. 197, 11 (citing *Amgen Inc. v. Sanofi, Aventisub LLC*, 987 F.3d 1080 (Fed. Cir. 2021)). The functional requirement in *Amgen* was the ability of a monoclonal antibody of any structure to bind the PCSK9 enzyme in any way at particular residues. 987 F.3d at 1083. Here, the functional requirements are far narrower: either increasing NAD^+ biosynthesis ('807 Patent) or improving or prolonging the health or well-being of an animal ('086 Patent) with a composition comprising NR or derivatives that can improve the transport and delivery of NR. Ex. 1, '807 Patent, 29:4-8. Elysium admits that NR can achieve these goals. *See, e.g.*, Ex. 8, ¶¶ 172, 176.

When, as here, there are multiple genuine disputes of fact, any one of which could affect the outcome of the enablement analysis, summary judgment is inappropriate. *Evonik*, 2016 WL 337378, at *8.

III. The specification provides adequate written-description support for the Asserted Claims.

The specification of the Dartmouth Patents provides a description that reasonably conveys to a POSA that the inventor was in possession of the claimed inventions at the time of filing. XSF3-19. A POSA would understand from the specification that the term derivative "reference[s] salts and esters of NR, which are well understood in the art to deliver the NR moiety following oral administration." Ex. 5, ¶ 1036. A POSA would also understand without further explanation which

esters and salts could be used to deliver NR. Ex. 4, ¶¶ 26-32. Nothing more is required to satisfy the written-description requirement. *See Alcon Res. Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1190-91 (Fed. Cir. 2014).

As in the enablement analysis, *Idenix* is inapposite. Unlike the thousands of unknown compounds with unknown biological activities in *Idenix*, derivatives of NR are a comprehensible class of compounds designed to deliver one compound, NR. *See* Ex. 4, ¶ 32. For example, a POSA would know from NR's cationic structure alone that derivatives of NR encompass salts. *See, e.g.*, Ex. 4, ¶ 31; Ex. 6, ¶¶ 15-16. It would have also been readily apparent from the specification that derivatives encompass esters. *See, e.g.*, 28:58-29:10; Ex. 4, ¶¶ 26-30.

Elysium's argument that the Asserted Claims lack written-description support relies entirely on the purportedly massive scope of derivatives, on which there is a genuine dispute of fact. Elysium's motion for summary judgment should be denied because it cannot escape the genuine disputes of material facts underpinning these issues.

Dated: May 14, 2021

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WORD COUNT CERTIFICATION

The undersigned counsel hereby certifies that the foregoing brief complies with the type-volume limitations of paragraph 20(c) of the Scheduling Order (D.I. 40). The text of the brief, including footnotes, was prepared using Times New Roman 14-point font, and it contains 2,236 words (excluding the title, caption, tables, and signature block).

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CERTIFICATE OF SERVICE

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