

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SAREPTA THERAPEUTICS, INC.,

Petitioner

v.

GENZYME CORPORATION,

Patent Owner

U.S. Patent No. 12,031,894

“Analytical Ultracentrifugation for
Characterization of Recombinant Viral Particles”

IPR2026-00150

**PETITIONER’S AUTHORIZED RESPONSE TO PATENT OWNER’S
REQUEST FOR DIRECTOR REVIEW OF THE DECISION GRANTING
INSTITUTION**

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I. INTRODUCTION

The Director’s recent precedential guidance confirms that *inter partes* review serves an important public function in correcting improvidently granted patents and protecting the integrity of Patent Office proceedings. *Magnolia Med. Techs., Inc. v. Kurin, Inc.*, IPR2026-00097, Paper 17, 2-9 (Director May 14, 2026) (precedential). This case squarely implicates those concerns.

The Patent Office is uniquely situated to fix the errors that occurred during prosecution of U.S. Patent No. 12,031,894 (“the ’894 patent”). The challenged claims issued only after Genzyme persuaded the Examiner that the “linear relationship” between AAV sedimentation characteristics and genome size was previously unknown. However, Genzyme failed to disclose highly material prior art – published decades earlier – that directly teaches the linear relationship between these properties. The Board correctly instituted review because this case presents a straightforward example of apparent Examiner error resulting from materially misleading prosecution arguments. As such, the institution decision advances the public interest objectives identified by the Director in *Magnolia Medical*, and Genzyme’s request for Director review of the institution decision should be denied.

To overcome prior art cited during prosecution of the ’894 patent, Genzyme characterized the purported invention as the “discovery” of a linear relationship between two properties of AAV particles when analyzed by analytical

ultracentrifugation (“AUC”). The Examiner accepted Genzyme’s argument, and allowed the claims of the ’894 patent to issue.

Genzyme failed to disclose to the Examiner that the purportedly “previously unknown” linear relationship had been disclosed in the prior art as early as 1978 by AAV research pioneers Luis de la Maza and Barrie Carter. EX1007; EX1008. Genzyme led the Examiner astray by arguing that the named inventors were the first to recognize the linear relationship in 2015, and the Examiner was not made aware of key prior art references material to patentability. Every ground in the Petition cites de la Maza, which was not previously presented to the Office.

Rather than address the important issues of public interest and integrity of Patent Office proceedings, Genzyme’s request for Director review largely rehashes the arguments it unsuccessfully raised in its request for discretionary denial. Genzyme focuses heavily on the denial of institution of *other* petitions as a basis to reconsider the institution decision here. The purported burden on Genzyme does not override the Board’s interest in rectifying an Examiner error resulting from Genzyme’s misleading prosecution arguments.

Genzyme also raises Sarepta’s indefiniteness contentions for the first time on Director review. Notably, Genzyme did not raise this issue in its initial request for discretionary denial, even though Genzyme received Sarepta’s contentions more than three months earlier. But even if the Director were to consider Genzyme’s

indefiniteness arguments, there is no inconsistency between Sarepta’s indefiniteness contentions in the District Court and the obviousness grounds in the instant Petition. Instead, this case falls squarely within the example discussed in *Tesla*, which the Director has identified as acceptable. *Tesla, Inc. v. Intellectual Ventures II LLC*, IPR2025-00340, Paper 18, 3-4 (Director Nov. 5, 2025). Contrary to Genzyme’s arguments, it is Genzyme who is attempting to game the system by relying on misleading arguments during prosecution to obtain the ’894 patent claims, and then, attempting to sidestep Patent Office review of that allowance decision by reiterating its earlier unsuccessful arguments for discretionary denial in the pending request for Director review.

For these reasons, Genzyme’s request should be denied.

II. ARGUMENT

A. The ’894 Patent Grant Implicates the Integrity of Patent Office Proceedings

The ’894 patent presents a unique, straightforward case for IPR. The ’894 patent stands apart from other, unrelated patents at issue in the pending district court litigation. It is unique because of representations that Genzyme made to the Patent Office that resulted in the grant of the challenged ’894 patent claims. Genzyme’s representations put the integrity of the patent system squarely at issue, and thus the Patent Office is the correct forum to adjudicate the validity of the ’894 patent. “At

bottom, the central purpose of IPRs is to determine whether the patent at issue may have been improvidently granted and whether and to what extent that right should continue to be recognized at all.” *Magnolia Med. Techs.*, IPR2026-00097, Paper 17, 7. Genzyme’s representations caused the Examiner to err in granting the ’894 patent claims. Examiner error or oversight should be rectified by the Patent Office.

As detailed in Sarepta’s Petition, before filing the application that led to the ’894 patent, Genzyme was faced with two IPR petitions challenging the claims of U.S. Patent No. 10,429,288 (“the ’288 patent”), which issued from a grandparent application in the same family as the ’894 patent. Paper 2, 17-18. The two IPR petitions challenged all claims of the ’288 patent as anticipated and/or obvious in light of *Le Bec*, which had not been cited during prosecution. EX1016; EX1018, 2-3; EX1019, 2. In response, Genzyme disclaimed claims 4 and 10-14. EX1021, 2. The Board granted institution of both IPRs on all remaining claims, but later terminated the IPRs at the parties’ request due to settlement of the district court litigation. EX1020, 41; EX1021, 28; EX1022, 3.

While the IPRs for the ’288 patent were pending, Genzyme filed the continuation application that led to the ’894 patent, seeking narrower claims in the same family. EX1001, (21)-(22). The ’894 patent claims are limited to methods of quantifying species of rAAV particles comprising “fragmented” genomes, including

the step of “determining the genome size” of one or more species in the mixture. EX1001, 55:2-56:57.

During prosecution of the '894 patent, the Examiner rejected the pending claims as anticipated and/or obvious over Le Bec in combination with McLaughlin, Berkowitz (2007), or Cole. EX1002, 175-80. Genzyme argued that the key to the '894 patent was the discovery of the “linear relationship between sedimentation coefficients and molecular weights of genomes,” which allowed the inventors to determine the molecular weight (or size) of fragmented genomes using sedimentation coefficient data obtained via AUC. EX1002, 140, 146. The *only* distinction Genzyme drew between the '894 patent claims and Le Bec was that the “linear relationship between sedimentation coefficients and molecular weights of genomes was not disclosed in Le Bec.” *Id.*, 146.

De la Maza, which was not before the Examiner during prosecution, taught this allegedly distinguishing characteristic in a 1978 book chapter, more than 35 years before the '894 patent priority date. De la Maza explicitly teaches the correlation between “[t]he density of the incomplete virus particles” and “the size of the incomplete DNA” within the particles. EX1007, 203. As de la Maza explains in a subsequent article discussing the 1978 work, “the particle density has an approximately *direct linear relationship* to the strand length.” EX1008, 3202 (emphasis added).

Genzyme was aware of the foundational work conducted by de la Maza and Carter before filing the '894 patent. Indeed, Genzyme cites a different article from the Carter lab twice in the '894 patent specification. EX1001, 43:37-41 (citing EX1012), 45:18-21 (same). Despite this awareness, Genzyme did not cite the contemporaneous de la Maza articles characterizing AAV particles with fragmented genomes and explicitly teaching the direct linear relationship between particle density and genome size. Had de la Maza been disclosed during prosecution, the Examiner would not have accepted Genzyme's argument that the '894 patent inventors were the first to recognize the linear relationship between sedimentation coefficients and the molecular weights of fragmented genomes in AAV particles.

As explained in the Petition, de la Maza teaches the linear relationship between the *density* of an AAV particle and the size of the genome inside the capsid. EX1007, 203; EX1008, 3194, 3202; EX1011, 449. In turn, a POSA would have understood from the disclosure in de la Maza that there is a linear relationship between the *sedimentation coefficient* of an AAV particle and genome size. This relationship follows from the Svedberg equation, which describes the relationship between density and sedimentation coefficient and would have been well understood by a POSA at the relevant time. Paper 2, 45; EX1004, ¶¶41-42.

The Svedberg equation defines a particle's sedimentation coefficient as:

$$s = M (1 - \bar{v}\rho) / (N_a f)$$

where s is the sedimentation coefficient of the particle, M is the molar mass of the particle, $\bar{v}$ is the partial specific volume of the particle (inverse of particle density), ρ is the density of the solvent, N_a is Avogadro's number, and f is the frictional coefficient of the particle. Paper 2, 11; EX1004, ¶¶38-39.

As explained by Dr. Steven Berkowitz in his declaration supporting the Petition, because AAV particles have approximately the same size and shape, regardless of the size of the genome inside the capsid, the frictional coefficient for AAV particles is approximately constant for empty particles, particles containing full genomes, and particles containing fragmented genomes. EX1004, ¶41. Likewise, solvent density ρ is constant for a given solution at a given temperature. *Id.*, ¶42. Therefore, in a mixture of AAV particles “every parameter in the Svedberg equation is constant except for particle molar mass and partial specific volume (the inverse of density).” *Id.* De la Maza's experimental results confirm what the Svedberg equation predicts mathematically: sedimentation coefficient is directly proportional to mass and density for all intact monomeric AAV particles, which have approximately the same size and shape, regardless of the size of the genome packaged inside. *Id.*, ¶¶100-103. Thus, de la Maza – viewed by a POSA with background knowledge in the art as to the Svedberg equation – teaches the purportedly previously unknown linear relationship between sedimentation coefficient and genome size. The linear relationship between *sedimentation*

coefficient and genome size follows from the linear relationship between *density* and genome size disclosed in de la Maza for AAV particles, according to the Svedberg equation.

De la Maza was undisputedly not disclosed to the Office during prosecution. Genzyme misled the Examiner by arguing that the '894 patent inventors “discovered that sedimentation coefficients can be used to accurately calculate the molecular weight of [fragmented] genomes.” EX1002, 140. Genzyme’s failure to disclose the prior art teachings in de la Maza resulted in error material to the patentability of the '894 patent claims.

The appropriate forum to “correct a possible error in the original patent grant” is the Patent Office. *Magnolia Med. Techs.*, IPR2026-00097, Paper 17, 6; *see also id.* (“[T]he factors Congress requires the Director to consider in promulgating rules sound in the public interest,” including “the economy, efficient administration of the Office, the ability of the Office to timely complete its AIA reviews, and the integrity of the patent system.”). The purported burden to Genzyme created by the institution decision does not outweigh the strong public interest in the integrity of the patent system.

Genzyme’s cited cases do not suggest otherwise. Genzyme attempts to elevate the denial of institution as to other patents asserted in the parallel district court proceeding to an overriding factor that trumps all other discretionary factors.

Paper 19, 7-8 (citing *Samsung Elecs. Co. v. VB Assets, LLC*, IPR2025-00870, Paper 11 at 2-3 (PTAB Oct. 10, 2025), *Amazon.com, Inc. v. Audio Pod IP, LLC*, IPR2025-00768, Paper 15 at 3 (Director Aug. 14, 2025), and *Samsung Elecs. Co. v. ICashe, Inc.*, IPR2025-00641, Paper 12 at 3 (Director Aug. 14, 2025)).

None of Genzyme’s cited decisions support this assertion. Each decision was “based on a holistic assessment of all of the evidence and arguments presented.” *VB Assets*, IPR2025-00870, Paper 11 at 3; *Amazon.com*, IPR2025-00768, Paper 15 at 3; *ICashe*, IPR2025-00641, Paper 12 at 3. And each decision included factors not present here, such as settled expectations for the patent owner (*Amazon.com*, IPR2025-00768, Paper 15 at 2-3; *ICashe*, IPR2025-00641, Paper 12 at 2) and trial scheduled to occur before the projected Final Written Decision date (*VB Assets*, IPR2025-00870, Paper 11 at 3; *ICashe*, IPR2025-00641, Paper 12 at 2).

As Sarepta explained in its response to Genzyme’s discretionary denial request, trial in the District Court is currently scheduled to begin after the date for a Final Written Decision. Paper 13, 15. Likewise, Genzyme has no settled expectations because the ’894 patent issued on July 9, 2024 – the year before Sarepta petitioned for IPR. *Id.*, 19-20. The passage of time and denial of institution of IPRs for other patents asserted in the same District Court case do not change the outcome for the ’894 patent. Discretionary denial is inappropriate given the strong public interest factors present here.

B. The Institution Decision Advances Public Policy Considerations Identified in *Magnolia Medical*

The Director recently emphasized that discretionary institution analysis may appropriately take into account “American manufacturing and/or small business considerations” as part of the public interest analysis for IPR proceedings. *Magnolia Med. Techs.*, IPR2026-00097, Paper 17, 7. Those considerations further support institution here.

Sarepta Therapeutics is a biotechnology company at the forefront of precision genetic medicine – with substantial research, development, and manufacturing operations in the United States, including facilities in Massachusetts and Ohio. Sarepta has invested heavily in the development and commercialization of gene therapy products for the treatment of rare diseases, including FDA-approved therapies for Duchenne muscular dystrophy. The challenged patent is being asserted against Sarepta in connection with those domestic innovation and manufacturing activities.

This proceeding therefore implicates not only the integrity of Patent Office decision-making, but also the public interest in ensuring that patents asserted against domestic innovators were properly granted in the first place. As *Magnolia Medical* explains, the Director’s discretionary authority exists in part to ensure that IPR proceedings serve these broader public interests. *Id.*, 6-7.

Here, the Petition presents substantial evidence that the allowance of the '894 patent rested on an incomplete presentation of the prior art before the Examiner. Institution accordingly serves the public interest objective of permitting the Patent Office to reconsider whether the challenged claims should “continue to be recognized at all.” *Id.*, 7.

Genzyme’s request for Director review does not meaningfully address these public interest considerations. Instead, Genzyme repeats the same discretionary arguments previously presented to and rejected by the Office. The Director should decline Genzyme’s invitation to disturb that decision on institution.

C. Genzyme’s Arguments as to Sarepta’s Indefiniteness Contentions Are Untimely and Unsupported

In its request for Director review, Genzyme raises, for the first time, a new argument for discretionary denial regarding Sarepta’s indefiniteness contentions in the District Court. Paper 19, 10. Genzyme could have, but did not, raise this argument in its discretionary denial request. Paper 12. Genzyme skirts around this omission by arguing that its discretionary denial request “noted that Sarepta had raised §112 issues in its contentions.” Paper 19, 10 (citing Paper 12). However, the discretionary denial request merely notes that Sarepta raised §101 and §112 contentions in the District Court litigation. At no point did Genzyme suggest that

Sarepta’s indefiniteness contentions are inconsistent with the obviousness grounds raised in the Petition.

Director review is not intended to provide serial reconsideration of ordinary discretionary arguments that could have been presented earlier in the proceeding. Genzyme’s belatedly-raised arguments on indefiniteness undermine the objectives of Patent Office efficiency, conservation of resources, and predictability. *Magnolia Med. Techs.*, IPR2026-00097, Paper 17, 6. Thus, as an initial matter, Genzyme’s new indefiniteness argument should be rejected as an untimely second bite at the discretionary denial apple. *See also* Director Review Process at 3.E (“The Director will not consider new evidence or new arguments not part of the official record.”).¹

Genzyme’s untimely indefiniteness arguments also fail on the merits. As the Director explained in *Tesla*, a petitioner may simultaneously allege indefiniteness and obviousness where “notwithstanding the alleged indefiniteness of the claim term, an ordinarily skilled artisan would understand that the asserted art satisfies the claim limitation.” *Tesla*, IPR2025-00340, Paper 18, 3. Such is the case here.

In the District Court, Sarepta contends that the full scope of the term “boundary sedimentation velocity conditions” is indefinite. The ’894 patent specification defines this term to “refer to any experimental conditions under which

¹ <https://www.uspto.gov/patents/ptab/decisions/director-review-process>.

a sample solution is subjected to sedimentation velocity analysis.” EX2018, 43 (citing common specification of the ’326 patent, 17:29-32). To the extent that the claims of the ’894 patent purport to cover all experiments in which a sample is subjected to sedimentation velocity analysis, Sarepta contends the claims fail to delineate the claim scope with reasonable certainty because different experimental conditions and sedimentation velocity methods may yield different results for the same test sample. Thus, the outer limits of subject matter encompassed by this element are indefinite.

Here, the “boundary sedimentation velocity conditions” element which Sarepta alleges is indefinite falls squarely within the example discussed in *Tesla*. As in that case, the element at issue here “prescribe[s] a range and only the outer bounds of the range [are] unclear.” *Tesla*, IPR2025-00340, Paper 18, 3-4.

In the Petition, Sarepta explained that the asserted “prior art reads on the claims under *any* construction.” Paper 2, 33 (emphasis added). There is no dispute that the cited prior art Le Bec reference discloses a specific set of boundary sedimentation velocity conditions that falls within the scope of the claims. *Id.*, 40; EX1004, ¶¶150-155. By contrast, the indefiniteness dispute in the District Court will be focused on whether the outer bounds of the “boundary sedimentation velocity conditions” element are adequately defined. Thus, there is no inconsistency between

Sarepta's indefiniteness contentions in the District Court and its obviousness contentions in this proceeding.

Because this case falls within the example discussed in *Tesla*, Genzyme's citations to *AutoConnect* and *Terumo* are inapposite. Paper 19, 3, 10-12. In both cases, the Petitioner submitted indefiniteness contentions *after* institution was granted that were inconsistent with the plain and ordinary meaning construction advanced in the IPRs. *Ford Motor Co. v. AutoConnect Holdings, LLC*, IPR2025-01342, Paper 27, 3 (Director May 12, 2026); *Terumo BCT Inc. v. Haemonetics Corp.*, IPR2025-01374, Paper 20, 3 (Director May 12, 2026). By contrast here, Sarepta served its invalidity contentions in the district court case *before* filing its Petition, challenging the outer limits of a single claim element that does not implicate whether the cited prior art meets that claim limitation.

Finally, Genzyme rehashes the argument from its discretionary denial request that Sarepta should have filed a PGR to address all patentability issues for the '894 patent in a single forum. As Sarepta previously explained, Genzyme waited to file suit until after the PGR deadline. Paper 13, 18. Genzyme filed the original complaint in the District Court proceeding on July 26, 2024, but did not assert the '894 patent in District Court until May 27, 2025 – nearly two months after the PGR deadline. EX1050, 9 (D.I. 74, 75). Sarepta acted promptly to file its IPR Petition after Genzyme added the '894 patent to the Delaware case. Paper 2. Genzyme's

attempt to place the burden on Sarepta – and any entity receiving a notice letter – to preemptively undertake the time and expense of preparing and filing a PGR petition should be rejected.

III. CONCLUSION

The Board correctly instituted review because this proceeding advances the Director's stated public-interest objectives of correcting possible errors in patent grants, promoting the integrity and predictability of the patent system, and ensuring that IPR proceedings serve their intended purpose. Genzyme identifies no basis for disturbing that institution decision. Therefore, the request for Director review should be denied.

May 28, 2026

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. §42.6, I hereby certify that on May 28, 2026, the foregoing document, Petitioner's Authorized Response to Patent Owner's Request for Director Review of the Decision Granting Institution was served via email on the following counsel of record:

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