

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SAREPTA THERAPEUTICS, INC.,
Petitioners,

v.

GENZYME CORPORATION,
Patent Owner.

Case No. IPR2026-00150
Patent No. 12,031,894

PATENT OWNER'S REQUEST FOR DISCRETIONARY DENIAL

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2001	Declaration of Katherine A. Helm
2002	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 78 – Joint Stipulation to Amend Scheduling Order
2003	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 59 – Notice of Service of Plaintiff’s Initial Claim Charts on Infringement
2004	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 68 – Notice of Service of Defendant’s Initial Invalidity Contentions
2005	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 28 - Notice of Service of Plaintiff’s First Set of Requests for Production of Documents and Things
2006	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 35 - Notice of Service of Defendant’s First Set of Requests of Production of Documents and Things to Plaintiff and First Set of Interrogatories and Initial Disclosures
2007	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 37 - Notice of Service of Plaintiff’s Second Set of Interrogatories and Second Set of Requests for Production of Documents and Things
2008	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 45 – Notice of Service of Plaintiff’s First Set of Interrogatories and Third Set of Requests for Production of Documents and Things
2009	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 67 - Notice of Service of Defendant’s Second Set of Requests of Production of Documents and Things to Plaintiff and First Set of Interrogatories
2010	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 83 - Notice of Service of Defendant’s Amended Second Set of Requests of Production of Documents and Things to Plaintiff and First Set of Interrogatories
2011	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 87 - Notice of Service of Defendant’s Third Set of Requests of Production of Documents and Things to Plaintiff

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2012	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 91 – Notice of Service of Plaintiff’s Responses to Defendants Third Set of Requests for Production of Documents and Things
2013	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 92 - Notice of Service of Plaintiff’s Fourth Set of Requests for Documents and Things
2014	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 99 – Notice of Service of Plaintiff’s Fifth Set of Requests for Documents and Things
2015	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 102 – Notice of Service of Defendant’s Fourth Set of Requests of Production of Documents and Things to Plaintiff
2016	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 110 – Notice of Service of Plaintiff’s Sixth Set of Requests for Production of Documents and Things
2017	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) D.I. 76 – Second Amended Complaint
2018	<i>Genzyme Corporation v. Sarepta Therapeutics Inc.</i> (1:24-cv-00882) - Defendant’s Supplemental Initial Invalidity Contentions -
2019	Burnham et al., Analytical Ultracentrifugation as an Approach to Characterize Recombinant AAV Vectors, 26 <i>Human Gene Therapy Methods</i> 228 (2015) (“Burnham 2015”)
2020	F. Collaud et al., Preclinical Development of an AAV8-hUGT1A1 Vector for the Treatment of Crigler-Najjar Syndrome, 12 <i>Molecular Therapy: Methods & Clinical Development</i> 157, 166-67 (March 2019)
2021	E. Spies, Assessing the Quality of Adeno-Associated Virus Gene Therapy Vectors by Sedimentation Velocity Analysis, <i>AUC Insights</i> (March 2020)
2022	<i>Novartis Gene Therapies, Inc. v. Genzyme Corp.</i> , IPR2023-01044, Paper 12 (Jan. 23, 2024), Patent Owner’s Request for Rehearing by the Director
2023	US 2017/0362608 to McLaughlin et al. (“McLaughlin”)
2024	<i>Novartis Gene Therapies, Inc. v. Genzyme Corp.</i> , IPR2023-01044, Paper 1 (Jun. 1, 2023).

I. Introduction

Patent Owner Genzyme Corporation (“Genzyme”) respectfully requests discretionary denial of the *inter partes* review (“IPR”) Petition challenging U.S. Patent No. 12,031,894 (“’894 patent”) filed by Petitioner Sarepta Therapeutics, Inc. (“Sarepta”). This Petition presents a textbook case for discretionary denial. Sarepta seeks to relitigate issues already thoroughly examined while pursuing the same invalidity theories in parallel district court litigation racing toward trial.

The *Fintiv* factors, and the broader interests of judicial efficiency, compel discretionary denial under 35 U.S.C. § 314(a). The parallel Delaware district court litigation satisfies five of the six *Fintiv* considerations (factors 1-3, 5, and 6), which decisively favor denial. Trial is scheduled days after the projected final written decision (“FWD”)—virtually guaranteeing significant duplication. The district court and parties have already invested substantial resources in that litigation and continue to do so. Contentions and interrogatories have been exchanged, claim construction proceedings and document production will be complete before projected institution, and fact discovery closes shortly thereafter. Sarepta’s *Sotera* stipulation does not outweigh these compelling factors.

Maintaining parallel district court and IPR proceedings would waste valuable Board and district court resources, result in duplicative efforts, risk conflicting judgments, and unnecessarily prolong resolution of this dispute. The

district court is positioned to resolve this dispute comprehensively and expeditiously; an IPR would waste resources and risk inconsistent outcomes.

Sarepta also falls short of its burden to provide compelling new Grounds not covered during prosecution. The Petition relies heavily on the same primary reference, Le Bec, that was central to examination and overcome by Genzyme. The de la Maza reference, which Sarepta introduces and alleges was a “material omission” (Petition, 3), is cumulative of the art and arguments already cited during prosecution. Thus, Genzyme respectfully requests that the Board deny institution.

II. *Fintiv* and § 314(a) Strongly Favor Discretionary Denial

Discretionary denial under 35 U.S.C. §314(a) is appropriate to ensure that the resources of the Board, the district court, and the parties are not wasted on duplicative parallel proceedings. *General Plastic Indus. Co. v. Canon Kabushiki Kaisha*, IPR2016-01357, Paper 19 at 16 (PTAB Sept. 6, 2017) (“the goals of the AIA [are] namely, to improve patent quality and make the patent system more efficient by the use of post-grant review procedures.”). Applying the projected FWD date of June 4, 2027, five of the six *Fintiv* factors strongly favor denial of institution: (1) the district court will not stay the case, (2) trial is scheduled within days of the statutory FWD deadline, (3) the parties and district court have made significant investments in the district court proceeding, (5) the petitioner and defendant are the same party, and (6) the Petition’s merits are weak and duplicative

of examination. *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11 (PTAB Mar. 20, 2020) (precedential) (“*Fintiv*”). The remaining consideration, (4) Sarepta’s *Sotera* stipulation, does not outweigh the factors favoring discretionary denial.

A. *Fintiv* Factor 1 Favors Discretionary Denial Because the District Court Will Not Stay Its Case

The district court has not, and likely will not, stay its case. Months ago, two of the patents-in-suit, U.S. Patent Nos. 7,704,721 and 9,051,542, were challenged by Petitioner in IPRs but were denied institution by the Director. *Sarepta Therapeutics, Inc. v. Genzyme Corp.*, IPR2025-01194, 01195, Paper 15 (Director Nov. 20, 2025). Judge Andrews, the presiding District of Delaware judge, is unlikely to grant a stay because Sarepta’s current IPR filings cover fewer than all asserted patents. *Collabo Innovations, Inc. v. Sony Corp.*, No. 15-cv-1094-RGA, D.I. 43 (D. Del. Jan. 5, 2017) (“Some simplification will be achieved by the three IPRs, but the fourth patent and its claims will have to be litigated regardless.”); *Ansell Healthcare Prods. LLC v. Reckitt Benckiser LLC*, No. 15-cv-915-RGA, D.I. 105 (D. Del. Dec. 1, 2016) (stay denied because “[n]o IPR is sought on two of the four asserted patents.”); *RainDance Techs., Inc. v. 10X Genomics, Inc.*, No. 15-cv-152-RGA, D.I. 37, 38 (D. Del. Apr. 6, 2016) (stay denied after IPRs instituted for two of the six asserted patents). Factor 1 strongly favors discretionary denial.

B. *Fintiv* Factor 2 Favors Discretionary Denial Because Trial Is Scheduled Days After the Projected Final Written Decision Date

The jury trial in the Delaware litigation is scheduled to begin June 14, 2027,

and involves substantially the same claims that Sarepta challenges here. Ex. 2002.

This is merely ten days after the projected June 4, 2027 FWD is due, which creates substantial risk of duplicative efforts and inconsistent outcomes. Discretionary denial is favored “[i]f the court’s trial date is at or around the same time as the projected statutory deadline.” *Fintiv*, Paper 11 at 9.

The Director has similarly determined that when the trial date and FWD due dates are in such close proximity, factor 2 favors denial. The proximity of the trial date and FWD favors denial even though the scheduled trial date is slightly after the FWD date. *See Samsung Elecs. Co. v. VB Assets, LLC*, IPR2025-00870, Paper 11 at 2 (PTAB Oct. 10, 2025) (“[E]ven though a district court trial date that occurs after a projected final written decision date reduces the possibility of conflicting decisions, that benefit does not outweigh the efficiencies gained by avoiding parallel proceedings under these circumstances.”). The Board has found that factor 2 favors denial where, like here, trial is projected for the same month the FWD is due. *Shenzhen Tuozhu Tech. Co. v. Stratasy, Inc.*, IPR2025-00354, Paper 11 at 2 (PTAB June 12, 2025) (“[I]t will be inefficient to maintain two parallel proceedings when the district court scheduled trial date and the projected final written decision due date are in close proximity.”).

C. *Fintiv* Factor 3 Favors Discretionary Denial Because The Parties Have Expended Considerable Resources in the District Court

The parties have already invested significant resources and time in the

Delaware litigation. For the challenged patents, Genzyme has served infringement contentions (Ex. 2003), and Sarepta served its invalidity contentions (Ex. 2004).

The parties have served and responded to numerous rounds of interrogatories and requests for production (Exs. 2005-2016). Claim construction proceedings are well underway. The parties exchanged claim terms, proposed constructions, and filed a joint claim construction chart, all before Sarepta filed its Petition. Ex. 2002. The parties have already filed their opening and answering claim construction briefs.

Id. By June 4, 2026, the projected institution date, claim construction briefing will have concluded—the parties will have filed a joint claim construction brief and appeared for a claim construction hearing, presently scheduled for April 8, 2026.

Id. The deadline for substantial completion of document production, April 15, 2026, is months prior to projected institution. *Id.* Fact discovery closes shortly thereafter, on June 30, 2026. *Id.*

Such significant investment in the district court proceeding prior to the institution date favors discretionary denial, regardless of whether trial occurs days after the Board issues its FWD. *Be Smarter, LLC v. Yonder, Inc.*, IPR2025-00970, Paper 14 at 2 (Director Sept. 26, 2025) (“it is not clear whether a [FWD] will issue before the district court trial occurs. The parties, however, have made meaningful investments in the district court proceeding [T]he parties have exchanged infringement and invalidity contentions, and a Markman hearing is scheduled to

occur before the due date for an institution decision.”); *Ericsson Inc. v. Pegasus Wireless Innovation LLC*, IPR2025-00084, Paper 17 at 14 (Director June 6, 2025) (“significant investment in the parallel district court proceeding has already occurred. A claim construction hearing was held in the parallel district court proceeding Also, the parties have exchanged invalidity contentions.”); *Nokia of Am. Corp. v. Pegasus Wireless Innovation LLC*, IPR2025-00037, Paper 14 at 11-12 (PTAB Apr. 25, 2025) (factor 3 weighed in favor of discretionary denial when “[t]he parties have exchanged contentions and the district court has held its *Markman* hearing fact discovery is (or soon will be) closed, and the parties are set to exchange initial expert reports.”).

D. *Fintiv* Factors 5 and 6 Further Favor Discretionary Denial

Factor 5 also favors discretionary denial. Sarepta is the Petitioner and a defendant in the Delaware Litigation. The other defendant, Sarepta Therapeutics Three, LLC, is a wholly-owned subsidiary of Sarepta. Genzyme is the Patent Owner and the only plaintiff in the Delaware Litigation. *Samsung Elecs. Co. v. SiOnyx, LLC*, IPR2025-00065, Paper 16 at 16 (Director June 6, 2025).

Factor 6, which allows the Board to consider “other circumstances” that may impact its discretion, further favors discretionary denial. As explained above, the Board has already denied institution as to two of the patents in the Delaware litigation, U.S. Patent Nos. 7,704,721 and 9,051,542. Ex. 2017; *Sarepta*, IPR2025-

01194, 01195, Paper 15. The Board has repeatedly held that it is inefficient to institute an IPR after it has denied institution as to other patents from the same parallel proceeding. *See VB Assets*, IPR2025-00870, Paper 11 at 2-3 (“there are six patents at issue in the parallel district court proceeding, the two patents challenged in these proceedings and four patents challenged in other petitions filed by Petitioner, in which institution was denied . . . In view of this, Patent Owner persuasively argues that addressing all of the challenged patents in the district court proceeding would be ‘the fastest and most efficient resolution of the Parties’ many disputes.”); *Amazon.com, Inc. v. Audio Pod IP, LLC*, IPR2025-00768, Paper 15 at 3 (Director Aug. 14, 2025) (“the district court will be considering the validity of the patents challenged in [other IPRs where institution was denied], along with the validity of the patent challenged in IPR2025-00768, and referring IPR2025-00768 to the Board would be an inefficient use of Board resources and tips the balance to discretionary denial as to that patent too.”); *Samsung Elecs. Co. v. ICashe, Inc.*, IPR2025-00641, Paper 12 at 3 (Director Aug. 14, 2025) (same).

Finally, Sarepta’s art and arguments fail to raise new issues not considered during examination. *Infra* § III. Repeating cumulative art and arguments to those Genzyme overcame during prosecution reflects the weak merits of the Petition.

E. The *Sotera* Stipulation Does Not Outweigh Other Considerations

Sarepta’s *Sotera* stipulation does not cure the inefficiency of maintaining

parallel proceedings. A March 24, 2025 memorandum from then Chief Judge Boalick explained that although a *Sotera* stipulation remains “highly relevant” for discretionary considerations, it is “not ... dispositive by itself.” Boalick at 2-3. Maintaining this IPR proceeding in parallel to the district court litigation would be highly inefficient. Sarepta’s *Sotera* stipulation restricts it from raising arguments it could have raised under §§ 102 and 103 based on patents, printed publications, and system art. But Sarepta’s invalidity contentions in the district court litigation are far more expansive and include §§ 101 and 112 arguments. Ex. 2018.

On July 26, 2024 and October 31, 2024, Genzyme notified Sarepta of its concern that Sarepta was infringing the ’894 patent based on Sarepta’s activities relating to its Elevidys[®] product and offered it a license to the ’894 patent. Ex. 2017, ¶¶ 54-56, Exhibit I. From Genzyme’s first notice, Sarepta had over eight months to prepare and file a PGR challenge before the nine-month deadline of April 9, 2025. Sarepta, however, delayed its IPR filing until sixteen months after Genzyme first notified Sarepta of the ’894 patent. While Sarepta delayed challenging the ’894 patent, the Delaware case proceeded, leading the parties to invest time and resources in the district court. Instituting IPR would now be a duplicative and inefficient parallel proceeding. Sarepta’s *Sotera* stipulation does not outweigh the many factors that favor denial of institution.

Sarepta could have raised these arguments in a timely filed PGR. Instead, it

waited and filed an IPR with its more limited estoppel provisions. Unlike PGR estoppel, which bars a petitioner in an instituted PGR from making any invalidity arguments under any statutory basis in district court (35 U.S.C. § 325(e)(2)), Sarepta's *Sotera* stipulation leaves Sarepta unencumbered from pursuing its § 101 and § 112 contentions. *See, e.g., Motorola Sols., Inc. v. Stellar, LLC*, IPR2024-01205, Paper 19 at 3-4 (PTAB Mar. 28, 2025) (vacating institution decision despite *Sotera* stipulation because "Petitioner's invalidity arguments in the district court are more expansive"); *Shenzhen Tuozhu*, IPR2025-000354, Paper 11 at 2-3 (denying institution despite *Sotera* stipulation based on petitioner's broad invalidity contentions in district court).

III. Discretionary Denial Under § 325(d) Is Also Warranted

The Petition relies heavily on the same reference, *Le Bec* (Ex. 1006), that was a focus of prosecution. Sarepta contends that a reference published in 1978, *de la Maza* (Ex. 1007), "was a material omission" that resulted in allowance of the claims. But the Petition does not explain how the omission of *de la Maza* was a material error during prosecution when references considered by the Examiner supplied the same teachings. Far from being a material omission, *de la Maza* is merely cumulative and adds nothing of substance to what the Examiner already considered. Discretionary denial under § 325(d) is therefore warranted. *See Advanced Bionics, LLC v. Med-El Electromedizinische Geräte GmbH*, IPR2019-

01469, Paper 6 at 7 (PTAB Feb. 13, 2020) (precedential) (“*Advanced Bionics*”);
see also Becton, Dickinson & Co. v. B. Braun Melsungen AG, IPR2017-01586,
Paper 8 at 17 (PTAB Dec. 15, 2017) (precedential as to § III.C.5, first paragraph)
 (“*Becton, Dickinson*”).

A. The ’894 Patent’s Disclosure and Independent Claims

The ’894 patent claims methods for the identification and quantification of rAAV viral particle species by analytical ultracentrifugation under boundary sedimentation velocity (“SV-AUC”). Ensuring an adequate amount of full capsids is critical for viable gene therapies. The ’894 patent claims the use of SV-AUC to determine the amount of DNA contained in rAAV viral particle species (*e.g.*, empty capsids, partially filled capsids, and full capsids), and the relative concentrations of these different species in a mixture. Ex. 1001, 21-25. With the ’894 patent’s instruction, the person of ordinary skill in the art (“POSA”) can use SV-AUC to analyze a rAAV particle mixture to determine the amount of genetic material in each rAAV particle species by determining the sedimentation coefficient (S) of each species and correlating the S value to molecular weight. Ex. 1002, 139-40.

The Examiner allowed the ’894 patent (*id.*, 21-30) after Genzyme explained that the inventors discovered a previously unknown linear relationship between the molecular weight and AUC sedimentation coefficient of rAAV particles:

The inventors ... discovered that sedimentation coefficients can be used to accurately calculate the molecular weight of the genomes in every viral particle of the preparation, including the molecular weights of the fragmented genomes. The linear relationship between sedimentation coefficients and molecular weights of genomes was not disclosed in Le Bec. For at least this additional reason, Le Bec and the cited prior art does not teach or suggest claim 99, as amended or any claim depending from claim 99.

Id., 146; *see also* Ex. 1001, 9:36-40. Independent claim element 1(iii) (claim element 96(iii)) recites “determining the genome size of one or more species of the individual variant viral particles in the heterogeneous mixture of viral particles.”

Id., 140-41.

As an example of the claimed invention, Example 5 describes making a standard curve plot correlating the number of packaged nucleotides of known rAAV species with their sedimentation coefficients.

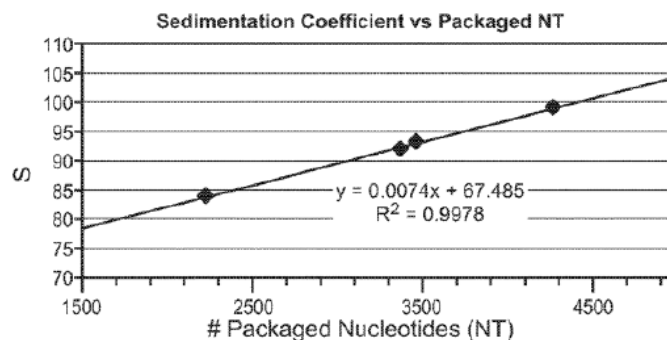


FIG. 8

Ex. 1001, Fig. 8; *see also id.*, 142. The standard curve makes it possible to analyze unknown rAAV species having genomes of differing sizes and determine the

number of nucleotides packaged in each unknown species. *Id.*, 49:57-50:41; 45:1-

8. By determining the molecular weight of rAAV particles in a mixture of particles, it also becomes possible to calculate the relative concentrations of each species in the mixture. *Id.*, 50:43-67, Figs. 9A, 9C (Example 5); Ex. 1002, 140.

Independent claim element 1(iv) (claim element 96 (iv)) recites “determining the quantity of one or more species of the variant viral particles in the heterogeneous mixture of viral particles.”

In a January 18, 2024 non-final rejection, the Examiner rejected the pending claim 96 (claims 1 of the '894 patent) as anticipated and obvious. The Examiner explained that Le Bec “fails to teach generation of a standard curve to determine the size of AAV particles with genomes in unknown AAV samples” but that “all of these steps would be routine optimization steps to one of skill in the art, as evidenced by the teachings of McLaughlin, Cole, and [Berkowitz (2007)].” Ex. 1002, 177. The Examiner explained that the prior art “teach[es] expected sedimentation coefficients for empty and full AAV were known, thus giving a reasonable expectation of success to a skilled artisan in generating a standard curve of other viral particles based on sedimentation coefficients, thus rendering the limitations ... obvious.” *Id.*, 180.

In its April 18, 2024 response, Genzyme responded that the cited references do not teach ““determining the genome size of one or more species of the

individual variant viral particles in the heterogeneous mixture of viral particles’ or ‘determining the quantity of one or more species of the variant viral particles in the heterogeneous mixture of viral particles.’” *Id.*, 144. Moreover, because the sedimentation coefficient depends on multiple factors including “molecular weight ... and also on molecular shape,” the POSA would not have expected there to be a linear correlation between sedimentation and molecular weight. *Id.*, 145-46; *see also id.*, 140. After Genzyme’s response, the claims were allowed on May 2, 2024. *Id.*, 21.

The Examiner also considered prior petitions challenging U.S. Patent 10,429,288 (“’288 patent”), the grandparent of the ’894 patent, IPR2023-01044 and -1045 (“’288 patent IPRs”). Those petitions raised similar arguments to those that Sarepta makes here relating to the correlation between sedimentation coefficient and molecular weight. *Id.*, 32, 190. The Examiner allowed the ’894 patent despite those arguments.

B. *Advanced Bionics* Part 1: Sarepta Relies Identical and Cumulative Prior Art and Arguments

1. All Grounds of the Petition Rely on Le Bec

The Petition fails *Advanced Bionics* part one by asserting art and arguments that both overlap and are cumulative with those that Genzyme overcame during prosecution of the ’894 patent. *Advanced Bionics*, Paper 6 at 9 n.10 (citing *Becton, Dickinson*, Paper 8 at 17–18). The Petition relies primarily on Le Bec for all

elements of independent claim 1. Le Bec was the focus of obviousness and anticipation rejections overcome by Genzyme during prosecution (Ex. 1002, 174-80; *supra* § II.A). *Advanced Bionics*, Paper 6 at 10; *Becton, Dickinson*, Paper 8 at 18-21 (factor (a)). For claim elements 1(iii) and 1(iv), the Petition alleges that the Examiner's allowance of the claims was a material error because the Examiner "was not aware of" de la Maza (Ex. 1007), which when combined with Le Bec allegedly renders these elements obvious. Petition, 3; Ex. 1004, ¶ 82.

2. De la Maza's Disclosure Is Cumulative

De la Maza adds nothing new that was not already taught in the references cited by the Examiner and overcome by Genzyme, including Berkowitz (2007) (Ex. 1023), McLaughlin (Ex. 2023), and Cole (Ex. 1009). Ex. 1002, 142-46. Like de la Maza, these references do not expressly disclose a correlation between sedimentation coefficient and rAAV particle molecular weight. De la Maza is "similar and cumulative in the evidentiary context of disclosure" to what was of record during prosecution. *Becton, Dickinson*, Paper 8 at 22 (factor (b)).

For example, Sarepta's obviousness argument for claim elements 1(iii) and 1(iv) fails because the prior art already disclosed the alleged "missing" teaching. Sarepta states that "[d]e la Maza teaches that there is a linear relationship between the density of an AAV particle and the size of the DNA packaged within the capsid." Petition, 43 (citing Ex. 1007, 203), 67 (citing Petition § IX.A.21). The

Petition further alleges that “[a]pplying the teachings of de la Maza to the SV-AUC methods in Le Bec, a POSA would have been able to determine the size of fragmented genomes as a function of the sedimentation coefficients of the AAV particles.” *Id.*, 45.

But the examination record already included multiple references teaching this same correlation between genome size and viral particle density, but lacking in the correlation between genome size and sedimentation coefficient. First, Berkowitz (2007) disclosed that adenoviral particles subjected to sedimentation equilibrium AUC (“SE-AUC”) in CsCl produce a density gradient where empty capsids are less dense (1.29–1.32 g/mL) than full/intact virus particles (1.34–1.35 g/mL). Ex. 1023, 20. This is the identical technique that de la Maza used to determine AAV particle densities. *Compare* Ex. 1007, 194.

Second, McLaughlin explains that “[i]ntermediate replicative species are successfully packaged in virus particles” (Ex. 2023, [0074]) and that “[q]uantitation of the relative amounts of [scAAV] intermediate species is determined by densitometry.” *Id.*, [0399]. Third, Le Bec states that “[k]nowing that the difference in density is sufficiently significant to distinguish them by centrifugation, we have implemented a method today for analytically separating by ultracentrifugation and quantifying the different species present in an AAV viral preparation.” Ex. 1006, 18:1-6. Thus, the examination record already includes

several disclosures indicating a correlation between genome size and viral particle density. De la Maza adds nothing new.

What de la Maza fails to disclose—just like Le Bec, Berkowitz (2007), and McLaughlin—is a connection between the ***sedimentation coefficient*** and rAAV molecular weight. The de la Maza and Berkowitz (2007) analyses were conducted with sedimentation equilibrium AUC (“SE-AUC”), which is different from SV-AUC. The Berkowitz Declaration admits that the distribution of particles in SE-AUC “is a function of its buoyant mass” and is not impacted by other factors known to impact a particle’s sedimentation coefficient. Ex. 1004, ¶ 31 (citing Ex. 1024, 241). Berkowitz (2015) contrasts the claimed method of SV-AUC with SE-AUC. Berkowitz (2015) explains that SE-AUC is “independent of [the particle’s] hydrodynamic shape (which plays an important role in SV-AUC experiments)” and “totally independent of the frictional properties of the protein molecule.” Ex. 1024, 241. For this reason, “[molecular weight] assessment via SV-AUC [is] much more difficult.” *Id.* Thus, a POSA would not have been able to simply assume a linear correlation between a particle’s density/molecular weight and sedimentation coefficient. As Berkowitz (2015) explains, shape and frictional properties impact its sedimentation coefficient. Hence, a POSA would have understood that de la Maza, just like the references considered by the Examiner, including Berkowitz (2007), do not linearly correlate sedimentation coefficient and molecular weight.

C. *Advanced Bionics* Part 2: Sarepta Fails to Identify a Material Error in Prosecution

Sarepta cannot overcome § 325(d) by merely identifying a reference not previously cited. The cumulative references were not “simply listed in an IDS during prosecution,” they formed the basis a rejection. *Becton, Dickinson*, Paper 8 at 23 (factor(c)). *Le Bec*, Berkowitz (2007), McLaughlin, and Cole were substantively considered in prior art rejections. Ex. 1002, 174-80. Thus, *Le Bec* and the cumulative references were considered in depth during prosecution.

1. Sarepta’s Material Error Allegation Is Conclusory

Sarepta makes sweeping but unsupported allegations: that the lack of citation to *de la Maza* was a “material omission that allowed Patent Owner to overcome the Examiner's rejections” and that the Examiner “was led astray by Patent Owner’s argument that the named inventors were the first to recognize the linear relationship between sedimentation coefficients and the molecular weights of fragmented genomes.” Petition, 3. These conclusory statements cannot satisfy Sarepta’s burden to demonstrate material error. Critically, the Petition never explains how *de la Maza* provides additional information that the references cited by the Examiner do not provide. For example, the Petition never addresses the fact that *de la Maza* and Berkowitz (2007) teach density-genome size correlation using identical AUC techniques. *Supra* § II.B.2

2. Sarepta Fails to Address the Examiner's Analysis

Sarepta “has not pointed to error by the Examiner, or for that matter addressed the evidence and argument presented by Patent Owner, during the underlying prosecution of the [challenged patent].” *Becton, Dickinson*, Paper 8 at 24-25. Without such an explanation, “Petitioner’s arguments that the Office made a material error during prosecution are not persuasive.” *Apple Inc. v. Advanced Coding Techs. LLC*, IPR2025-00983, Paper 10 at 3 (Director Oct. 3, 2025). This failure to engage with the art the Examiner actually considered and Genzyme's prosecution arguments is fatal to overcoming § 325(d).

3. The Examiner Allowed the Claims Over Flawed Arguments From the '288 Patent IPR that Sarepta's Petition Recycles

Sarepta's obviousness theory suffers from the same fundamental flaw that undermined the '288 patent IPR petition. Both petitions assume that “particle shape and friction can be disregarded”—the very factors Berkowitz (2015) states cannot be disregarded. *Supra* § II.B.2 (citing Ex. 1024, 241).

Sarepta argues: “a POSA would understand that the size and shape of intact, non-aggregated AAV particles are approximately the same, regardless of the size of the genome packaged in the capsid.” Petition, 45. The '288 Patent IPR argued that “[i]n a hypothetical system where the rAAV particles are uniform and have an identical frictional coefficient, the sedimentation coefficient (*s*) will be proportional to the effective particle mass.” Ex. 2024, 46. Both arguments rely on

the identical flawed assumption that particle shape and friction are negligible—an assumption the prior art explicitly contradicts.

The Examiner considered these arguments, having signed off as having “reviewed” all papers of the ’288 patent IPR (Ex. 1002, 32, 190). Thus, Sarepta’s arguments overlap significantly with the arguments made in the ’288 Patent IPR that were considered by the Examiner in allowing the ’894 patent. The inclusion of de la Maza provides “little if any, different argument than that considered previously by the Office.” *Becton, Dickinson*, Paper 8 at 24.

IV. Institution of the ’288 Patent IPR Does Not Favor Institution Here

The institution of the ’288 patent IPR (Petition, 17-18) should have no bearing on this proceeding. *First*, Genzyme overcame the institution decision and the records of two ’288 patent IPRs during examination. Ex. 1002, 38, 188. Sarepta fails to identify a compelling reason to second guess the Examiner. *Second*, the institution decision was erroneous. The Board mistakenly applied the wrong standard of review, finding that a “genuine issue of material fact” favored institution. See *Novartis Gene Therapies, Inc. v. Genzyme Corp.*, IPR2023-01044, Paper 12 (Jan. 23, 2024) (Ex. 2022). The presumption favoring the petitioner that the decision relied on was eliminated in a 2020 rule change. *Id.*, 2-7. Had the IPRs not settled, the Board would likely have been required to reconsider institution. Thus, the prior institution decision provides no basis for institution here.

V. Industry Recognition of the Claimed Invention Provided Genzyme with Settled Expectations

Although the '894 patent issued in 2024, industry adoption of its technology created some settled expectations for Genzyme. *Cf. Alliance*, IPR2025-00950, Paper 11 (Technology licensing can create settled expectations). Companies in the AUC and gene therapy spaces have acknowledged the importance of the claimed AUC method. A 2015 peer-reviewed publication co-authored by the inventors of the '894 patent, Burnham and O'Riordan, publicized experiments in the '894 patent and covered by its claims. Ex. 2019 ("Burnham 2015"). Beckman Coulter GmbH, a leading AUC instrument manufacturer, cited Burnham 2015 to highlight the importance of the patented invention resulting in AUC becoming "a valuable tool to analyze rAAV vectors." Ex. 2021 (citing *id.*). A 2018 publication by gene therapy company, Genethon, and co-authored by the first named inventor of Ex. 1006, Christine Le Bec, cited Burnham 2015 for its AUC "method that has been demonstrated to provide a reliable readout." Ex. 2020, 166-67 (citing Ex. 2019). This recognition weighs in favor of discretionary denial.

VI. Conclusion

For the foregoing reasons, Genzyme respectfully requests that the Petition be discretionarily denied, and no proceeding instituted.

Dated: February 4, 2026

/Blaine M. Hackman /

Blaine M. Hackman, Reg. No. 67,479
Counsel for Patent Owner

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), I certify that today in

Sarepta Therapeutics, Inc., v. Genzyme Corporation, IPR2026-00150

I caused to be served a copy of:

PATENT OWNER'S REQUEST FOR DISCRETIONARY DENIAL

EXHIBIT NOS. 2002-2024

upon:

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Date: February 4, 2026

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