Trials@uspto.gov
571-272-7822

Paper 9
Date: April 14, 2021

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

EVERGREEN THERAGNOSTICS, INC.,
Petitioner,

v.

ADVANCED ACCELERATOR APPLICATIONS SA,
Patent Owner.

PGR2021-00002
Patent 10,596,278 B2

Before SHERIDAN K. SNEDDEN, ZHENYU YANG, and JAMIE T. WISZ, *Administrative Patent Judges.*

YANG, *Administrative Patent Judge.*

DECISION
Denying Institution of Post-Grant Review
35 U.S.C. § 325(d)

INTRODUCTION

Evergreen Theragnostics, Inc. ("Petitioner") filed a Petition (Paper 2 ("Pet.")), requesting a post-grant review of claims 1–25 of U.S. Patent No. 10,596,278 B2 (Ex. 1002, "the '278 patent"). Advanced Accelerator Applications SA ("Patent Owner") filed a Preliminary Response (Paper 7 ("Prelim. Resp.")).

We review the Petition under 35 U.S.C. § 324, which provides that a post-grant review may not be instituted unless "it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable." 35 U.S.C. § 324(a). For the reasons provided below, we exercise our discretion to deny institution of post-grant review under 35 U.S.C. § 325(d).

Related Matters

Petitioner also filed PGR2021-00001, challenging the same claims of the '278 patent.[1] Pet. 80. Petitioner further filed PGR2021-00003, challenging the claims of U.S. Patent No. 10,596,276, a patent in the same family as the '278 patent. *Id.*

Background of the Technology and the '278 Patent

The '278 patent relates to "radionuclide complex solutions of high concentration and of high chemical stability, [which] allows their use as drug product for diagnostic and/or therapeutic purposes." Ex. 1002, Abstract.

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[1] The parties filed separate papers, addressing the issue of parallel petitions. Papers 3, 8. Because we deny the instant Petition for different reasons, we do not discuss that issue.

The targeted drug delivery concept has been used in radiomedicine to deliver radionuclides selectively to the target cells for diagnostic or therapeutic purposes. *Id.* at 1:35–37. In a radiomedicine application, a target cell receptor binding moiety is linked to a chelating agent that is able to form a strong complex with the metal ions of a radionuclide. *Id.* at 1:38–41. When the radiopharmaceutical drug is delivered, the decay of the radionuclide affects only the target cells. *Id.* at 1:41–44.

Specifically, peptide receptor radionuclide therapy (PRRT) was developed because "[n]early all cancers have overexpression of specific receptors on the tumor surface." Ex. 1016, 2951.[2] "The most widely employed modality of PRRT uses somatostatin analogues for targeting somatostatin receptors, which are overexpressed in neuroendocrine cancer." *Id.* ^{177}Lu is a therapeutic radionuclide (*id.* at 2939), and DOTA is one of the most widely used chelating agent for Lu (*id.* at 2940). Thus, ^{177}Lu-labeled-DOTA-somatostatin analogues, including ^{177}Lu-DOTA-TATE and ^{177}Lu-DOTA-TOC have been used in PRRT. *Id.* at 2952.

The '278 patent explains that,

> One technical problem with those radiopharmaceutical drug products is that the decay of the radionuclide occurs constantly, e.g. also during the manufacturing and during storage of the drug product, and the released high energy emissions induce the cleavage of the chemical bonds of the molecules which form part of the drug product. This is often referred to as radiolysis or radiolytic degradation. The radiolytic degradation of the receptor

[2] Unless otherwise noted, we cite the original page numbers of the exhibits.

> binding moiety of the drug may lead to a decrease in its efficacy to act as a diagnostic and/or therapeutic.

Ex. 1002, 1:45–54.

The '278 patent states that, before its invention, the usage of radiopharmaceutical drugs was limited due to their poor stability and the lack of any significant shelf-life. *Id.* at 1:55–2:8. Although prior art taught various ways to reduce radiolysis and improve stability of radiopharmaceutical drugs, each of those strategies has its own drawbacks. *Id.* at 2:9–39.

According to the '278 patent,

> It remains therefore a challenge to design a ready-to-use radiopharmaceutical drug product which can be produced at commercial scale and delivered as a sufficiently stable and sterile solution in a high concentration which leads to a for patient convenient small infusion volume and which has a composition of high physiological tolerability (e.g. a composition which does not contain ethanol).

Id. at 2:40–47.

The '278 patent states that its inventors "found a way to design and produce a highly concentrated radionuclide complex solution which is chemically and radiochemically very stable even if stored at ambient or short term elevated temperatures so that it can be produced on commercial scale and supplied as ready-to-use radiopharmaceutical product." *Id.* at 2:50–55.

Illustrative Claim

Independent claim 1 is illustrative of the challenged claims and is reproduced below:

1. A pharmaceutical aqueous solution comprising:

(a) a complex formed by

(ai) the radionuclide ^{177}Lu (Lutetium-177), and

(aii) a somatostatin receptor binding peptide linked to the chelating agent DOTA; and

(b) at least two different stabilizers against radiolytic degradation comprising

(bi) gentisic acid or a salt thereof; and

(bii) ascorbic acid or a salt thereof;

wherein

said radionuclide is present in a concentration that it provides a volumetric radioactivity of from 250 to 500 MBq/mL;

said stabilizers are present in a total concentration of from 1.0 to 5.0 mg/mL; and the pharmaceutical aqueous solution has less than 1% ethanol, and the radiochemical purity (determined by HPLC) of the solution is maintained at ≥95% for at least 72 h when stored at 25 °C.

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