UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BAYER CROPSCIENCE LP AND MONSANTO COMPANY,
Petitioners,

v.

CORTEVA AGRISCIENCE LLC,
Patent Owner

IPR2023-01038
U.S. Patent No. 11,299,745

PETITIONERS' AUTHORIZED REPLY TO PATENT OWNER'S PRELIMINARY RESPONSE

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I. Section 325(d) Denial Is Not Warranted for Grounds IA-B

A. Patent Owner argues under part one of *Advanced Bionics* that the issue of written description (and thus priority) arose during the '406 application prosecution. Paper 8 at 61-62 (collecting cites). The argument is misplaced. One of the most if not the most heavily emphasized arguments in the Preliminary Response about written description was *not* raised in prosecution, showing that the arguments in this proceeding are not substantially the same as those previously presented. *See Becton Dickinson* factor (d) (considering, *inter alia*, Patent Owner's IPR arguments). Patent Owner's newfound theory—made no fewer than seven times, without any expert testimony—is that written description comes from unsupported statements that "85-98%" is "highly identical" and "[t]raditionally only sequences with high homology would be expected to have similar properties to the input sequence." *E.g.*, Paper 8 at 40 (citing EX1003, 44:21-24); *id.* at 3, 10, 28, 31-32, 34, 41. Yet Patent Owner's citations show it did not assert in prosecution that such language supported the claims, relying on it instead to counter a § 103 rejection. Paper 8 at 61-62; EX1008, -492, -509, -576, -683-84; EX1011, -5434. Even if citation to such language in a § 103 argument somehow meant it was "presented," any reliance on it for written description would have been error. It refers to "α-ketoglutarate dioxygenase activity" in general, EX1003, 44:14-15, not *R*-enantioselectivity as the claims require, discussed *infra* 2-3. That is shown in the fact that the 27% conservation value is in

reference to tfdA, which has *S*-enantioselectivity. EX1003, 44:9-39; EX1008, -492 (AAD-1 "about 27%" to tfdA); Paper 8 at 56; EX1054, ¶¶ 54, 73-74, 489. Also, the statement about "similar properties" is wrong: Dr. Wright showed that a change to R285 alone eliminated αKG dioxygenase activity. EX1008, -474; Paper 2 at 32-34.

B. Patent Owner ignores Petitioner's contention that the examiner erred under *Advanced Bionics* because he relied on legally irrelevant information. Paper 2 at 32, 66-67. Rather, it makes several points to try to show there was no error because the examiner allegedly used the correct priority date. Paper 8 at 62-63. None has merit.

1. Patent Owner relies on ¶ 9 of Dr. Nair's declaration and its discussion of whether the AAD-1 motif was "readily apparent"—a discussion that points to the "conserved amino acids relevant" to αKG dioxygenase activity. Paper 8 at 62-63; EX1008, -594, ¶ 9. But, as Patent Owner recognizes, those conserved residues were shared by diverse αKG dioxygenases, and αKG dioxygenases have diverse stereo- and substrate selectivities—*e.g.*, tfdA has *S*-enantioselectivity; AAD-1/RdpA has *R*-enantioselectivity. EX1003, 3:36-41, 3:51-54; 8:19-25, 18:39-51; Paper 8 at 7-8, 56. Crucially, the claims do not recite a generic αKG dioxygenase activity, as Patent Owner suggests. They require *R*-stereospecific activity, *i.e.*, the ability to degrade *R*-FOPs and phenoxy auxin herbicides, which include *R*-phenoxy auxins (*see* claim 10). The Petition and Dr. Hausinger's declaration repeatedly make that point. *See* Paper 2 at 26, 29, 37-38; EX1054, ¶¶ 72-75, 87-91, 94-110, 489, 491. But the

specification does not identify the structures responsible for such enantiospecific activity on those substrates. Paper 2 at 26, 29, 37-38. Nor could it. The 2019 article cited in ¶ 11 of Dr. Nair's declaration—an article co-authored by inventor Wright—concedes that the structural features responsible for *R*-enantioselectivity not only were unknown prior to obtaining the crystal structure described therein, but also fall outside the claimed AAD-1 motif. EX1019, 13300-03; Paper 2 at 37-38. That undermines any support for the claims' functional requirements, showing error.

In addition, the part of Nair Declaration ¶ 9 cited by Patent Owner in its § 325(d) discussion ignores that arginine (R) at position 285 is required for activity—a point highlighted in Dr. Wright's first declaration and noted in the Petition. *See* EX1008, -474; Paper 2 at 32-34. That too establishes material error, as the AAD-1 motif does not require R285. Indeed, it is unsurprising that Dr. Nair never opined that R285 was "readily apparent." *See* Paper 8 at 62-63. The specification does not disclose that such an arginine is required, nor is it part of the prior-art motif or the AAD-1 motif. Paper 2 at 26, 34; EX1003, 18:39-19:5. That further shows error, and undercuts Patent Owner's reliance on Dr. Nair's declaration for § 325(d).

2. Patent Owner (at 63) improperly conflates the consensus prior art motif with the AAD-1 motif. It then asserts (*id.*) that Petitioners "concede" a POSA would recognize the AAD-1 motif, an allegation the Petition refutes (*e.g.*, at 24, 28-29).

3. Patent Owner's § 325(d) discussion relies on the citation to *Ajinomoto Co.*

v. ITC, 932 F.3d 1342 (Fed. Cir. 2019) during prosecution, and faults Petitioner for not addressing it. Paper 8 at 63. But Patent Owner omits that the examiner never cited the decision, suggesting it was unpersuasive. Even if the examiner had relied on *Ajinomoto*, it would only reinforce material error. Patent Owner's citation to *Ajinomoto* rests on a purported "correlation" between five active site residues and αKG dioxygenase activity. EX1008, -677-78; Paper 8 at 3, 31-32. But as noted in the Petition and discussed above, the claims do not require some kind of generic αKG dioxygenase activity—they require *R*-stereospecific αKG dioxygenase activity on particular substrates. However, the specification contains no identification of the structural features responsible for that activity. Paper 2 at 26, 29, 37-38.

4. Patent Owner alleges in its § 325(d) discussion that the Board has rejected what it labels as Petitioners' "numerosity theory" as discussed in § V(A)(2) of its Preliminary Response. Paper 8 at 62-63. As an initial matter, it is wrong to describe Petitioners' arguments as a mere "numerosity theory." The Petition does not rely on the number of embodiments alone. Rather, the number of embodiments reinforces that the three example enzymes—SEQ ID NO: 9 and two with ~99% identity—occupy a tiny "corner" of a massive genus that extends to 85% identity. Paper 2 at 31. Patent Owner cannot assert that the specification discloses examples anywhere near 85% identity. Paper 2 at 38-41. Patent Owner's "numerosity theory" label also rings hollow given its own focus on whether there are more than three examples,

Paper 8 at 37 (in § V(A)(2)), 62-63, which in any event ignores that the examples involve the same three enzymes, and the enzymes provide the activity.

The above demonstrates why the Board decisions Patent Owner cross-references from § V(A)(2) in its § 325(d) discussion (Paper 8 at 63) do not support discretionary denial. In *Campbell*, the specification disclosed an antibody with 87% identity, which helped support a claim with a lower limit of 90% identity. No. 2021-000865, Decision on Appeal (PTAB July 20, 2021), 15 n.3. By contrast, the specification here does not disclose an enzyme anywhere near the lower limit of 85% identity. In *Lifescan*, the specification "identifie[d] a portion of the claimed sequence believed to be critical to its activity." PGR2019-00032, Paper 11 (PTAB Aug. 15, 2019), 32. There is no disclosure here of what structures provide *R*-stereospecificity.

II. Section 325(d) Denial Is Not Warranted for Grounds IIA-B

Patent Owner asserts Saari 1998 is cumulative over Saari 1999. Paper 8 at 61. Not so. Patent Owner denies a prior art link between FOPs and phenoxy auxins, *id.* at 57, but Saari 1998 (Scheme 3) shows them side by side, in a discussion about herbicide degradation, EX1040, 7-12. That is not in Saari 1999. Patent Owner also alleges lack of error by criticizing the Petition's inherency arguments, referencing a Monsanto application about whether RdpA is "inactive" at the extreme condition of 46ºC. Paper 8 at 48-49, 63-64. Its argument wrongly posits that biological activity can never be inherent. *In re Montgomery*, 675 F.3d 1375, 1381 (Fed. Cir. 2012).

October 6, 2023

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CERTIFICATE OF SERVICE

I hereby certify that on October 6, 2023, I caused the foregoing Petitioners' Authorized Reply to Patent Owner's Preliminary Response to be served on counsel for Patent Owner via e-mail at:

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