Errata to FDA Briefing Document

Meeting of the Oncologic Drugs Advisory Committee (ODAC)

October 4, 2023

This erratum contains corrections to FDA's briefing information for the October 4, 2023 ODAC Meeting. The committee will discuss new drug application (NDA) 215500 for eflornithine (DFMO), submitted by US World Meds, for the following proposed indication: to reduce the risk of relapse in pediatric patients with high-risk neuroblastoma who have completed multiagent, multimodality therapy.

1. On page 19, under the header "Study 3(b): Investigational Arm," the first sentence of the second paragraph currently reads:

   "Stratum 1, which provided the primary efficacy data for the experimental arm of the ECT, enrolled 105 patients who were in remission at the end of up-front therapy defined as chemotherapy (5-7 cycles), surgery as indicated, consolidation therapy as indicated, radiation therapy as indicated, or anti-ganglioside 2 (GD2) antibody therapy with retinoic acid up to 6 cycles."

   The sentence should read:

   "Stratum 1, which provided the primary efficacy data for the experimental arm of the ECT, enrolled 105 patients who were in remission at the end of up-front therapy defined as chemotherapy (5-7 cycles), surgery as indicated, consolidation therapy as indicated, radiation therapy as indicated, **and** anti-ganglioside 2 (GD2) antibody therapy with retinoic acid up to 6 cycles."

2. On page 25, in the "Prior Therapy" row of Table 3, the third bullet currently reads:

   "Patients were enrolled no later than Day 100 after PBSC infusion."

   The third bullet should read:

   "Patients were enrolled no later than Day **200** after PBSC infusion."

3. On page 49, under the discussion of Efficacy Issue #3: Clinical Studies, the first sentence of the first paragraph currently reads:

"Study NMTRC002 (NCT 01059071) was a multi-center, single-arm, dose-escalation study of DFMO monotherapy administered for one cycle followed by DFMO plus oral etoposide, enrolled between 2010 and 2014 (Saulnier Sholler et al, 2015)."

The sentence should read:

"Study NMTRC002 (NCT 01059071) was a multi-center, single-arm, dose-escalation study of DFMO monotherapy administered for one cycle, followed by DFMO plus oral etoposide, enrolled between 2010 and **2012** (Saulnier Sholler et al, 2015)."

4. On page 50, under discussion of Efficacy Issue #3, the section describing Study NMTRC003(b) reads:

   "Study NMTRC003(b) also included Stratum 2. This stratum enrolled 35 patients with HRNB in remission after any previous relapse or refractory therapy. Patients had a median of one prior anti-cancer therapies (range 1-3) with a median of approximately one month between completion of last anti-cancer treatment and start of DFMO (range 4 to 124 days)."

   This section should read:

   "Study NMTRC003(b) also included Stratum 2. This stratum enrolled 35 patients with HRNB in remission after any previous relapse or refractory therapy. Patients had a median of one prior **relapse** therapies (range 1-3) with a median of approximately one month between completion of last anti-cancer treatment and start of DFMO (range 4 to 124 days)."

5. On page 50, under discussion of Efficacy Issue #3, the section describing Study NMTRC006 reads:

   "Study NMTRC006 (NCT03581240) is an ongoing expanded access study for patients with relapsed rare tumors with increased LIN28 expression, MYCN amplification, or upregulation of ornithine decarboxylase, including high-risk neuroblastoma…. Expanded access data regarding tumor responses or duration of remission in HRNB and related tumor types are challenging to interpret given the lack of pre-specified response criteria and imaging assessments and of a control arm."

   This section should read:

   "Study NMTRC006**b** (NCT03581240) is an ongoing expanded access study for patients with relapsed rare tumors with increased LIN28 expression, MYCN amplification, or upregulation of ornithine decarboxylase, including high-risk neuroblastoma…. Expanded access data regarding tumor responses or duration of remission in HRNB and related

tumor types are challenging to interpret given the lack of pre-specified response criteria and of a control arm."

6. On page 53, in Section 3.2.2, Safety Summary, the third paragraph reads:

   "In the primary safety population (N=85), the most common (≥5%) adverse reactions, including laboratory abnormalities, were otitis media, diarrhea, cough, sinusitis, pneumonia, upper respiratory tract infection, conjunctivitis, vomiting, pyrexia, allergic rhinitis, decreased neutrophils, increased ALT, increased AST, hearing loss, skin infection, and urinary tract infection (Table 13 and Table 14)."

   The paragraph should read:

   "In the primary safety population (N=85), the most common (≥5%) adverse reactions, including laboratory abnormalities, were otitis media, diarrhea, cough, sinusitis, pneumonia, upper respiratory tract infection, conjunctivitis, vomiting, pyrexia, allergic rhinitis, decreased neutrophils, increased ALT, increased AST, hearing loss, skin infection, and urinary tract infection (**Table 16 and Table 17**)."

7. On page 63, in the Appendix, the Table heading on page 63 reads:
   "Table 2020: Adjusted Event-free Survival hazard ratios comparing DFMO vs. NO DFMO adjusting for an unmeasured binary confounder having a hazard ratio of 2.0 and the observed hazard ratio in the current trial of 0.48."

   The table heading should read:

   "**Table 20:** Adjusted Event-free Survival hazard ratios comparing DFMO vs. NO DFMO adjusting for an unmeasured binary confounder having a hazard ratio of 2.0 and the observed hazard ratio in the current trial of 0.48."