UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

APOTEX INC.,
Petitioner,

v.

CELGENE CORPORATION,
Patent Owner

Case IPR2023-00512
Patent 8,846,628

EXPERT DECLARATION OF JEFFREY ETTER, PHD

CELGENE 2054

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I, Jeffrey B. Etter, Ph.D., declare as follows:

I. INTRODUCTION

1. I have been retained by counsel for Celgene Corporation ("Patent Owner") in connection with *Apotex Inc. v. Celgene Corporation*, No. IPR2023-00512, challenging claims 1, 2, 6-9, 11-28, 32-36, and 38-43 of U.S. Patent No. 8,846,628 ("the '628 patent").

2. I am a named inventor on '628 patent, along with my former colleagues at Pharmion Dr. Mai Lai and Dr. Jay Thomas Backstrom. Ex.1001('628 patent). I understand that Apotex Inc. ("Apotex") has filed an *Inter Partes* Review (IPR) at the USPTO challenging claims 1, 2, 6-9, 11-28, 32-36, and 38-43 of the '628 patent. I have been asked to explain how I and my co-inventors developed the inventions described in the '628 patent.

3. I am being compensated for my time in connection with this matter at my standard consulting rate, which is $275.00 per hour. My compensation is not dependent in any way upon the substance of my testimony or the outcome of this matter.

II. QUALIFICATIONS AND EXPERIENCE

4. I earned my bachelor's degree with a major in chemistry from Franklin & Marshall College in 1982. I earned my Ph.D. in organic chemistry from the University of Colorado in 1987.

5. Since earning my Ph.D., I have spent over 30 years in the drug development industry, holding positions as Director of Analytical Development at Somatogen (1990-1998), VP of Manufacturing at RxKinetic (1998-2002), Director of Drug Product at Allos Therapeutics (2002-2004), Director of Drug Product at Pharmion (2005-2008), Director of Formulations at Celgene (2008-2009), and Director, Senior Director, VP, and Senior VP of Pharmaceutical Development at Clovis Oncology (2009-2023). This year, I formed and am the managing member of Etter CMC Consulting, LLC where I consult for various clients on the production and development of drug products.

6. My curriculum vitae, which lists my professional experience and qualifications in greater detail, is attached hereto as **Appendix A**.

III. BASIS OF OPINIONS

7. I have considered the materials listed in **Appendix B**.

IV. THE DEVELOPMENT OF NON-ENTERIC COATED TABLETS COMPRISING A THERAPEUTICALLY EFFECTIVE AMOUNT OF 5-AZACYTIDINE

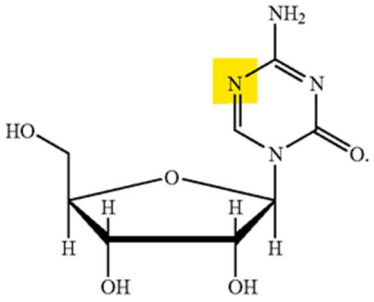
8. I was hired by Pharmion in 2004 to develop an oral formulation of 5-azacytidine to treat myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML or acute myelogenous leukemia). I worked closely with Dr. Mei Lai to develop oral formulations of 5-azacytidine, while Dr. Backstrom spearheaded the

clinical trials. Our work resulted in the inventions described in the '628 patent and the FDA-approved drug Onureg®. I describe our work in more detail as follows.

A. There Were Many Known Hurdles In Developing 5-Azacytidine As A Therapeutic.

9. In taking on the project of developing an oral formulation of 5-azacytidine, I was well aware of the known hurdles identified in the literature through decades of others trying to formulate 5-azacytidine.

10. 5-azacytidine is a nucleoside similar to the common nucleoside, cytidine. Ex.1001('628 patent), 2:37-62. 5-azacytidine has a nitrogen atom in place of a carbon atom present in cytidine, which is highlighted in the structure below (Ex.1001('628 patent), 2:48-62):



5-Azacytidine

11. 5-azacytidine was well-known as a promising anti-tumor drug since the 1960s. *See, e.g.*, Ex.2012(Čihák), 2091, 2100 (noting the compound's "pronounced… cancerostatic effects). After administration of 5-azacytidine, cancer cells will incorporate the nucleoside into DNA and RNA. *Id.*, 3:9-27. Upon incorporation, 5-azacytidine "restor[es] normal functions" by promoting "re-

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