## UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BLUEBIRD BIO, INC. Petitioner

v.

SLOAN KETTERING INSTITUTE FOR CANCER RESEARCH, Patent Owner

Patent No. 8,058,061

REPLY IN SUPPORT OF PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 8,058,061



#### **TABLE OF CONTENTS**

I.	Introduction1		
II.	Claims 1, 2, 5-7, and 11 Are Not Entitled to the Priority Dates of the Provisional Applications2		
	А.	No Written Description Support for All Globins and Their Mutations Covered by the Genus of Claims 1, 2, 5, 7, and 11	2
	B.	No Written Description Support for the Mutations and Non- human $\beta$ -globin Covered by the Genus of Claim 7	6
III.	The May Article Renders Claims 1, 2, 6-7, and 11 Obvious10		
	A.	SRT Confirms the Significant Motivation to Make TNS9	10
	B.	SRT Failed to Establish That the May Article Taught Away from Using Restriction Enzymes	13
	C.	SRT Failed to Establish That Dr. Bungert's Analysis Required Hindsight	15
	D.	SRT Is Incorrect That Dr. Bungert's Analysis Used Restriction Enzymes That a POSA Would Have Excluded	17
	E.	Dr. Riley's Own Analysis Confirms the Claimed HS Fragments Would Have Been Obvious	18
IV.	The May Abstract Renders the Challenged Claims Obvious		24
V.	SRT's Alleged Objective Indicia Only Confirms a POSA's Motivation to Make TNS9		29
VI.	Conclusion		30

### **TABLE OF AUTHORITIES**

#### Cases

<i>Ajinomoto Co. v. ITC</i> , 932 F.3d 1342 (Fed. Cir. 2019)	5
Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336 (Fed. Cir. 2010)	5
<i>In re Fulton</i> , 391 F.3d 1195 (Fed. Cir. 2004)	13
<i>In re Huai-Hung Kao</i> , 639 F.3d 1057 (Fed. Cir. 2011)	30
Mexichem Amanco Holdings v. Honeywell International, IPR2013-00576, Paper 36 (P.T.A.B. Sept. 5, 2014)	9
Novozymes A/S v. Dupont Nutrition Biosciences APS, 723 F.3d 1336 (Fed. Cir. 2013)	4
<i>Realtime Data, LLC v. Iancu,</i> 912 F.3d 1368 (Fed. Cir. 2019)	29
Schering Corp. v. Geneva Pharmaceuticals, 339 F.3d 1373 (Fed. Cir. 2003)	29

IPR2023-00074 Patent No. 8,058,061

Ex.1001	U.S. Patent No. 8,058,061 to Sadelain et al. ("the '061 patent")
Ex.1002	Declaration of Jörg Bungert, Ph.D.
Ex.1003	Curriculum Vitae of Jörg Bungert, Ph.D.
Ex.1004	May, "Therapeutic Hemoglobin Synthesis in Beta-Thalassemic Mice Expressing Lentivirus-Encoded Beta-Globin," Cornell University (2001) ("the <i>May Thesis</i> ")
Ex.1005	May, <i>et al.</i> , "Therapeutic Haemoglobin Synthesis in $\beta$ -thalassaemic Mice Expressing Lentivirus-Encoded Human $\beta$ -globin," Nature, 406:82-86 (2000) ("the <i>May Article</i> ")
Ex.1006	May, <i>et al.</i> , "Lentiviral-Mediated Transfer of the Human $\beta$ -Globin Gene and Large Locus Control Region Elements Permit Sustained Production of Therapeutic Levels of $\beta$ -Globin in Long-Term Bone Marrow Chimeras," Mol. Therapy, 1(5):S248-249 (2000) ("the <i>May</i> <i>Abstract</i> ")
Ex.1007	Perutz, <i>et al.</i> , "Hemoglobin Structure and Respiratory Transport," Sci. Am., 239(6): 92-125 (1978)
Ex.1008	Thein & Rochette, "Disorders of Hemoglobin Structure and Synthesis," <i>in</i> Principles of Mol. Med. 179 (Jameson, ed., 1998)
Ex.1009	Bank, et. al, "Disorders of Human Hemoglobin," Science, 207:486-93 (1980)
Ex.1010	He & Russell, "Expression, Purification, and Characterization of Human Hemoglobins Gower-I ( $\zeta_2 \epsilon_2$ ), Gower-2 ( $\alpha_2 \epsilon_2$ ), and Portland-2 ( $\zeta_2 \beta_2$ ) Assembled in Complex Transgenic-Knockout Mice, Blood, 97(4):1099-1105 (2001)
Ex.1011	Bunn, "Pathogenesis and Treatment of Sickle Cell Disease," N. Engl. J. Med., 337(11):762-69 (1997)

#### LIST OF EXHIBITS

IPR2023-00074 Patent No. 8,058,061

Ex.1012	Hardison, <i>et al.</i> , "Locus Control Regions of Mammalian β-globin Gene Clusters: Combining Phylogenetic Analyses and Experimental Results to Gain Function Insights, Gene, 205:73-94 (1997)
Ex.1013	Civin, <i>et al.</i> , "Sustained, Retransplantable, Multilineage Engraftment of Highly Purified Adult Human Bone Marrow Stem Cells <i>In Vivo</i> ," Blood, 88(11):4102-09 (1996)
Ex.1014	High, "Gene Therapy in Haematology and Oncology," <i>Lancet</i> , 356:S8 (2000)
Ex.1015	Ellis, <i>et al.</i> , "Evaluation of β-globin Gene Therapy Constructs in Single Copy Transgenic Mice," Nucleic Acids Res., 25(6):1296-1302 (1997)
Ex.1016	Li, <i>et al.</i> , "Nucleotide Sequence of 16-Kilobase Pairs of DNA 5' to the Human ε-Globin Gene," J. Biol. Chem., 260(28):14901-10 (1985)
Ex.1017	Mishima, <i>et al.</i> , "The DNA Deletion in an Indian $\delta\beta$ -thalassaemia Begins One Kilobase From the <sup>A</sup> $\gamma$ Globin Gene and Ends in an L1 Repetitive Sequence," Br. J. Haemotol., 73:375-79 (1989)
Ex.1018	Vosberg, "Molecular Cloning of DNA: An Introduction Into Techniques and Problems," Hum. Genet. 40(1):1-72 (1977)
Ex.1019	Roberts, "Restriction Enzymes and Their Isoschizomers," Nucleic Acids Res., 15(Suppl.):r189-r217 (1987)
Ex.1020	Zufferey, <i>et al.</i> , "Multiply Attenuated Lentiviral Vector Achieves Efficient Gene Delivery <i>in Vivo</i> ," Nature Biotech., 15:871-75 (1997)
Ex.1021	Miyoshi, <i>et al.</i> , "Transduction of Human CD34 <sup>+</sup> Cells that Mediate Long-Term Engraftment of NOD/SCID Mice by HIV Vectors," Science, 283:682-86 (1999)
Ex.1022	Sadelain, <i>et. al.</i> , "Generation of a High-titer Retroviral Vector Capable of Expressing High Levels of the Human β-Globin Gene," Proc. Natl. Acad. Sci. USA, 92:6728-32 (1995)

## DOCKET A L A R M



# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## **Real-Time Litigation Alerts**



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## **Advanced Docket Research**



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## **Analytics At Your Fingertips**



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

#### LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

#### FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

#### E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.