CRISPR Therapeutics, Intellia Therapeutics, Caribou Biosciences and ERS Genomics Provide Update on CRISPR/Cas9 U.S. Patent Interference Proceedings and Grants of Corresponding Patents in the U.K.

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- **UC'S PATENT APPLICATION COVERING THE USE OF CRISPR/CAS9 GENOME EDITING TECHNOLOGY WITH A SINGLE-GUIDE RNA FORMAT IN ANY NON-CELLULAR OR CELLULAR SETTING, INCLUDING HUMAN AND OTHER EUKARYOTIC CELLS, WILL BE RELEASED FROM THE INTERFERENCE ABSENT AN APPEAL, AND MAY THEN BE PROSECUTED TO POTENTIAL ISSUANCE**
- **ADDITIONAL LEGAL CHANNELS ARE AVAILABLE TO RECOGNIZE THE PRIORITY OF THE UNIVERSITY OF CALIFORNIA/UNIVERSITY OF VIENNA/CHARPENTIER INTELLECTUAL PROPERTY COVERING EUKARYOTIC CELLS**
- **U.S. PATENT TRIAL & APPEAL BOARD DID NOT MAKE A DETERMINATION REGARDING WHICH PARTY IN THE INTERFERENCE IS THE FIRST INVENTOR OF THE USE OF THE CRISPR/CAS9 GENOME EDITING TECHNOLOGY IN EUKARYOTES**
- **U.K. INTELLECTUAL PROPERTY OFFICE GRANTS PATENTS TO CRISPR/CAS9 GENOME EDITING TECHNOLOGY IN ANY CELLULAR SETTING – INCLUDING IN EUKARYOTES – TO UNIVERSITY OF CALIFORNIA/UNIVERSITY OF VIENNA/CHARPENTIER**

BASEL, Switzerland, CAMBRIDGE, Mass., BERKELEY, California, DUBLIN, Ireland, Feb. 15, 2017 (GLOBE NEWSWIRE) -- CRISPR Therapeutics (NASDAQ:CRSP), Intellia Therapeutics, Inc. (NASDAQ:NTLA), Caribou Biosciences, Inc., and ERS Genomics Limited provide an update on the Patent Trial & Appeal Board ("PTAB") of the U.S. Patent and Trademark Office ("USPTO") decision on the motions filed by the University of California, the University of Vienna and Dr. Emmanuelle Charpentier (collectively, "UC"), on one hand, and the Broad Institute, Harvard University and the Massachusetts Institute of Technology (collectively, "Broad"), on the other, in the interference proceeding relating to CRISPR/Cas9 genome editing technology ("CRISPR/Cas9 Technology"). The PTAB discontinued the current interference finding that the claim sets presented by the two parties were considered "patentably distinct" from each other because UC's current claims are broader in scope in that they are not restricted to use in eukaryotic cells, whereas Broad's claims are all limited to use in eukaryotic cells. As a result of the decision, UC's broader case, which was previously considered allowable but for the interference, is now released from the interference and may be prosecuted to potential issuance by UC, while a new interference can be sought with respect to eukaryote claims, currently pending in a separate UC patent application once they are deemed allowable. Alternatively, UC could appeal the current decision, which is currently under consideration. In parallel cases, the United Kingdom's Intellectual Property Office (UK IPO) granted patents to foundational CRISPR/Cas9 genome editing technology in any non-cellular or cellular setting (including in human cells) to UC.

The prosecution and enforcement of UC's foundational intellectual property covering CRISPR/Cas9 Technology, such as this patent application, is governed by a global cross-consent and invention management agreement between the co-owners of the intellectual property – the Regents of the University of California, Emmanuelle Charpentier, and the University of Vienna – as well as their key licensees and sublicensees – CRISPR Therapeutics, ERS Genomics, Caribou Biosciences, and Intellia Therapeutics.

U.S. Interference Proceeding

The written decisions and associated documents relating to U.S. patent interference 106,048 are publicly available at https://acts.uspto.gov/ifiling/PublicView.jsp.

- UC's earliest patent application describing the CRISPR/Cas9 genome editing technology was filed on May 25, 2012, and Broad's earliest patent application was filed on December 12, 2012.
- The interference was based on (i) UC's claims directed to the use of the CRISPR/Cas9 Technology with the widely used single-guide RNA format (in which the two key RNA molecules, tracrRNA and crRNA, are fused into a single molecule) in any setting – including but not limited to eukaryotic cells, and (ii) Broad's claims covering the use of the CRISPR/Cas9 Technology in eukaryotic cells only. UC's claims, which USPTO examiners previously deemed in condition for allowance subject to the interference, are now released from the interference, and UC may pursue them to potential issuance.
- The current proceeding was terminated as a "threshold" matter based on uses in eukaryotic cells being considered separately patentable from the use of the CRISPR/Cas9 Technology in all cellular and non-cellular settings (i.e. prokaryotes, eukaryotes and in vitro). Although UC's and Broad's claims both encompass uses in eukaryotic cells, the PTAB decided that the interference should not proceed with the current claim sets because UC's claims are broader in scope in that they are not limited to use in the eukaryotic setting, whereas Broad's claims are all limited to uses in eukaryotes. Under patent interference rules, the PTAB applies a "2-way" test requiring that the parties' claims define the "same patentable invention." In its decision, the PTAB concluded that, although they overlap, the respective scope of UC and Broad's claims did not define the same patentable invention.
- The PTAB's holding ends the current proceeding based on the patent claims before it, and the PTAB's decision is not intended to nor does it establish which party actually invented first with respect to use of the CRISPR-Cas9 Technology in eukaryotic cells. UC is free to seek a new interference with Broad's patents based on existing applications UC already has before the PTO that include claims limited to use of the CRISPR-Cas9 Technology in eukaryotes. If a new interference is sought and declared, it would then begin with a motions phase related to the newly-designated claims.
- The PTAB did not rule on substantive motions, including whether the parties are entitled to rely on their earliest patent applications for priority benefit. UC's earliest application was filed on May 25, 2012, and Broad's was filed on December 12, 2012. However, determinations on certain substantive matters have recently been made in parallel prosecution before

the USPTO. The USPTO has rejected a series of patent applications filed by Broad that are directed to uses of CRISPR/Cas9 Technology in eukaryotic cells (as in the claims involved in the interference) as being “non-novel” in view of the UC’s prior-filed patent application (which the USPTO examiners considered to have provided an enabling disclosure that effectively taught use of the CRISPR/Cas9 Technology in eukaryotic cells). These Broad cases include USSN 14/105,031, USSN 14/105,035, USSN 14/523,799, and USSN 14/703,511, all of which stand rejected by the USPTO. In rejecting Broad’s applications, the USPTO concluded that the UC’s priority application “discloses methods of, and compositions and CRISPR-Cas systems for interfering with a target DNA sequence in both prokaryotic and eukaryotic cells using CRISPR RNA (crRNA) and a CRISPR-associated (cas) protein/nucleic acid.” The USPTO also determined that Broad’s attempt to antedate or “swear behind” the earlier-filed UC patent applications using inventor declarations (as was done in obtaining many of the issued Broad patents) is improper because the UC case “clearly discloses each of the claimed limitations in the earliest two priority applications.” (Cf. Final Rejection of Broad application USSN 14/523,799, August 29, 2016, and similar rejections made against all of the other above-referenced Broad cases.)

- Regarding Staphylococcus aureus Cas9, the PTAB did not decide Broad’s substantive motion to “de-designate” (i.e. remove from the interference) claims directed to use of S. aureus Cas9 (essentially based on Broad’s arguments that use of the S. aureus Cas9 orthologue was non-obvious in view of the S. pyogenes Cas9 and therefore separately patentable). However, in substantive examination of an UC patent application, the USPTO recently determined as follows: “It would have been obvious to one of ordinary skill in the art to have modified the method of Jinek [a June 2012 publication co-authored by UC scientists] by replacing the S. pyogenes Cas9 protein with the Staphylococcus aureus Cas9 protein because it would have merely amounted to a simple substitution of one known Cas9 protein for another to yield predictable results.” (Cf. USPTO Official Action in USSN 14/942,782, January 4, 2017)

U.K. Patent Grants

Outside the United States, a UC application directed broadly to the single-guide CRISPR/Cas9 genome editing system (i.e. not limited by cellular or non-cellular setting) was examined by the United Kingdom’s Intellectual Property Office and, despite multiple evidentiary “observations” filed by third parties including the Broad, was granted as UK Patent No. 2518764. A second UK patent application, which is directed to chimeric CRISPR/Cas9 systems, was also the subject of third-party observations, and was granted as a patent on February 7, 2017 (UK Patent No. 2537000). Corresponding applications are being prosecuted in the European Patent Office and in other regional and national offices covering approximately 80 jurisdictions worldwide. Granted patents can be subject to proceedings challenging their grant, validity or scope.

Almost all jurisdictions worldwide are “first-to-file” systems, which recognize the first patent applicant(s) as the legal inventor(s) and do not permit the filer of a later patent application to antedate the earlier filings of others. In the case of the CRISPR-Cas9 Technology, UC filed its first priority application on May 25, 2012, and Broad filed more than six months later on December 12, 2012. In the United States, with respect to patent applications filed prior to March 2013, a subsequent filer could claim to have invented before an earlier filer by filing a declaration in the USPTO, which is what the Broad did and led to the interference proceeding discussed herein.

Broad’s related European patents have been opposed by numerous parties on procedural as well as substantive grounds, and are now the subject of proceedings challenging their validity and issuance at the Opposition Division of the European Patent Office.

About CRISPR Therapeutics

CRISPR Therapeutics is a leading gene-editing company focused on developing transformative gene-based medicines for serious diseases using its proprietary CRISPR/Cas9 gene-editing platform. CRISPR/Cas9 is a revolutionary technology that allows for precise, directed changes to genomic DNA. The Company’s multi-disciplinary team of world-class researchers and drug developers is working to translate this technology into breakthrough human therapeutics in a number of serious diseases. Additionally, CRISPR Therapeutics has established strategic collaborations with Bayer AG and Vertex Pharmaceuticals to develop CRISPR-based therapeutics in diseases with high unmet need. The foundational CRISPR/Cas9 patent estate for human therapeutic use was licensed from the Company’s scientific founder Emmanuelle Charpent
ier, Ph.D. CRISPR Therapeutics is headquartered in Basel, Switzerland with its R&D operations based in Cambridge, Massachusetts. For more information, please visit www.crisprtx.com.

About Intellia Therapeutics

Intellia Therapeutics is a leading genome editing company, focused on the development of proprietary, potentially curative therapeutics using the CRISPR/Cas9 system. Intellia believes the CRISPR/Cas9 technology has the potential to transform medicine by permanently editing disease-associated genes in the human body with a single treatment course. Intellia’s combination of deep scientific, technical and clinical development experience, along with its leading intellectual property portfolio, puts it in a unique position to unlock broad therapeutic applications of the CRISPR/Cas9 technology and create a new class of therapeutic products. Learn more about Intellia Therapeutics and CRISPR/Cas9 at intelliatx.com; Follow us on Twitter @intelliatweets.

About Caribou Biosciences, Inc.

Caribou is a developer of cellular engineering and analysis solutions based on CRISPR technologies. The Company was founded by pioneers of CRISPR/Cas9 biology based on research carried out in the Doudna Laboratory at the University of California, Berkeley. Caribou’s tools and technologies provide transformative capabilities to therapeutic development, agricultural biotechnology, industrial biotechnology, and basic and applied biological research. For more information, visit www.cariboubio.com and follow the Company @CaribouBio. “Caribou Biosciences” and the Caribou logo are registered trademarks of Caribou Biosciences, Inc.

About ERS Genomics

ERS Genomics was formed to provide broad access to the foundational CRISPR/Cas9 intellectual property held by Dr. Emmanuelle Charpentier. Non-exclusive licenses are available for research and sale of products and services across multiple fields including: research tools, kits, reagents; discovery of novel targets for therapeutic intervention; cell lines for discovery and screening of novel drug candidates; GMP production of healthcare products; production of industrial materials such as enzymes, biofuels and chemicals; and synthetic biology. For additional information please visit www.ersgenomics.com.

CRISPR Forward-Looking Statements

Certain statements set forth in this press release constitute “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the therapeutic value, development, and commercial potential of CRISPR/Cas-9 gene editing technologies and therapies and the intellectual property protection of our technology and therapies. You are cautioned that forward-looking statements are inherently uncertain. Although the company believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, the forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: uncertainties regarding the intellectual property protection for our technology and intellectual property belonging to third parties; uncertainties inherent in the initiation and completion of preclinical studies for the Company’s product candidates; availability and timing of results from preclinical studies; whether results from a preclinical trial will be predictive of future results of the future trials; expectations for regulatory approvals to conduct trials or to market products; and those risks and uncertainties described in Item 1A under the heading “Risk Factors” in the company’s most recent quarterly report on Form 10-Q, and in any other subsequent filings made by the company with the U.S. Securities and Exchange Commission (SEC), which are available on the SEC’s website at www.sec.gov. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. The information contained in this press release is provided by the company as of the date hereof, and, except as required by law, the company disclaims any intention or responsibility for updating or revising any forward-looking information contained in this press release.

Intellia’s Forward-Looking Statements

This press release contains “forward-looking statements” of Intellia within the meaning of the Private Securities Litigation Reform Act of 1995. These forward looking statements include, but are not limited to, statements regarding Intellia’s ability to advance CRISPR/Cas9 into therapeutic products for severe and life-threatening diseases and its CRISPR/Cas9 intellectual property portfolio, and statements regarding the intellectual property position and strategy of Intellia’s licensors. Any forward-looking statements in this press release are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, risks related to Intellia’s ability to protect and maintain its intellectual property position, risks related to the ability of Intellia’s licensors to protect and maintain their intellectual property position, the risk that any one or more of Intellia’s product candidates will not be successfully developed and commercialized, the risk of cessation or delay of any of the ongoing or planned clinical trials and/or development of Intellia’s product candidates, the risk that the results of previously conducted studies involving similar product candidates will not be repeated or observed in ongoing or future studies involving current product candidates, and the risk that Intellia’s collaborations with Novartis or Regeneron will not continue or will not be successful. For a discussion of other risks and uncertainties, and other important factors, any of which could cause Intellia’s actual results to differ from those contained in the forward-looking statements, see the section entitled “Risk Factors” in Intellia’s most recent quarterly report on Form 10-Q filed with the Securities and Exchange Commission, as well as discussions of potential risks, uncertainties, and other important factors in Intellia’s subsequent filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and Intellia Therapeutics undertakes no duty to update this information unless required by law.

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