CRISPR Therapeutics, Intellia Therapeutics, Caribou Biosciences and ERS Genomics Announce Appellate Brief Seeking Reversal of U.S. Patent Board Decision on CRISPR/Cas9 Gene Editing

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- **APPEAL SEEKS REVERSAL OF PATENT TRIAL AND APPEAL BOARD DECISION TERMINATING INTERFERENCE WITHOUT DETERMINING PRIORITY OF INVENTORSHIP OF CRISPR/CAS9 GENE EDITING**
- **BRIEF ASSERTS THAT THE BOARD FAILED TO PROPERLY APPLY CONTROLLING U.S. SUPREME COURT AND FEDERAL CIRCUIT PRECEDENTS, AND IGNORED EVIDENCE OF MULTIPLE GROUPS READILY APPLYING CRISPR/CAS9 GENE EDITING TO EUKARYOTIC CELLS FOLLOWING TEACHINGS OF CHARPENTIER-DOUDNA TEAM**

ZUG, Switzerland; CAMBRIDGE, Massachusetts; BERKELEY, California; DUBLIN, Ireland; July 25, 2017 (GLOBE NEWSWIRE) – CRISPR Therapeutics (NASDAQ:CRSP), Intellia Therapeutics, Inc. (NASDAQ:NTLA), Caribou Biosciences, Inc. and ERS Genomics, Ltd. announced that The Regents of the University of California, the University of Vienna, and Dr. Emmanuelle Charpentier (collectively "UC"), co-owners of foundational intellectual property relating to CRISPR/Cas9 genome engineering, today submitted an appellate brief to the U.S. Court of Appeals for the Federal Circuit (the "Federal Circuit") seeking reversal of a decision by the U.S. Patent and Trademark Office's Patent Trial and Appeal Board ("PTAB") in an interference proceeding relating to CRISPR/Cas9 gene editing technology. In the appeal, UC requests reversal of the PTAB's decision terminating the interference between certain CRISPR/Cas9 patent claims owned by UC and claims of the Broad Institute, Harvard University and the Massachusetts Institute of Technology (collectively, "Broad").

In its brief to the Federal Circuit (Case No. 17-1907), UC asserts that the PTAB's February 15, 2017 determination that the UC patent claims did not make the Broad's patent claims obvious is based on a misapplication of controlling legal standards established by U.S. Supreme Court and Federal Circuit precedent. In its decision, the PTAB had concluded that UC's claims covering CRISPR/Cas9 single guide gene editing technology and its application in any cellular or non-cellular setting did not make obvious Broad's claims covering application of the same technology limited to use in eukaryotic cellular settings.

In its brief, UC sets forth multiple errors in the PTAB's holding that the use of CRISPR/Cas9 in eukaryotes is separately patentable as alleged by Broad, including the following:

- With respect to the obviousness of applying the technology to eukaryotic cells, U.S. Supreme Court and Federal Circuit precedents clearly mandate that obviousness determinations be based on an "expansive and flexible approach" including consideration of "the inferences and creative steps that a person of ordinary skill in the art would employ." In contrast, the PTAB applied a narrow and restrictive approach that ignored certain key evidence, including the steps actually employed by those of skill in the art at the time, and also effectively required a "guarantee" that UC's CRISPR/Cas9 invention would work in eukaryotic cells, when well-established case law requires only a "reasonable expectation of success."
- With respect to the reasonable expectation of success standard that establishes obviousness, the PTAB effectively ignored U.S. Supreme Court and Federal Circuit case law, which emphasize that an invention can be obvious if it is "obvious to try," even if success is not guaranteed, "[w]hen there is a design need or market pressure to solve a problem," "there are a finite number of identified, predictable solutions," and experimentation leads to "the anticipated success."
- The PTAB ignored U.S. Supreme Court and Federal Circuit precedent highlighting that the occurrence of what appear to be simultaneous "inventions" arising close together in time is itself strong evidence of their obviousness, and accordingly requiring that such evidence be considered in any obviousness analysis. In contrast, in terminating the interference, the PTAB essentially dismissed as "irrelevant" the evidence that six different laboratories successfully applied UC's claimed CRISPR/Cas9 invention in eukaryotic cells using conventional techniques within months after UC publicly disclosed the invention - some of them prior to Broad's first filing.
- The PTAB effectively ignored that Broad's own eukaryotic application of UC's CRISPR/Cas9 invention had simply utilized conventional prior art techniques. As a consequence, it failed to consider that Broad's alleged invention did not reflect any significant innovation on Broad's part, an important issue under applicable precedent.
- The PTAB failed to hold Broad to its burden of proving, among other things, the effective priority date for its patent claims, as required by the PTAB's own rules and Federal Circuit precedent. By not requiring the Broad to meet its burden of proof, and by merely assuming that all of the Broad's claims were entitled to their earliest possible filing date despite Broad's failure of proof, the PTAB improperly ignored relevant intervening art that made the Broad's claims obvious.

As explained in UC's brief, application of the correct legal standards to the case is believed to require reversal of the PTAB's decision. For these reasons, UC requests that the Federal Circuit instruct the PTAB to reinstate the interference proceeding so that it can properly determine priority of inventorship, as previously requested by UC. The PTAB's failures to consider pertinent evidence and apply appropriate legal standards should at the very least require the matter to be remanded so that the PTAB can properly consider the evidence related to obviousness and Broad's no-interference-in-fact motion using appropriate legal standards.

In the PTAB's February decision terminating the interference proceeding prematurely, it had not yet considered the teachings of UC's own prior-filed patent application with respect to using CRISPR/Cas9 in eukaryotic cells. Instead, the PTAB only addressed the threshold question of whether use in eukaryotic cells can be separately patentable from use in all settings as covered by UC's claims. However, determinations on the underlying substantive matters have recently been made in parallel prosecution before the U.S. Patent & Trademark Office ("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 being non-novel in view of

UC's prior-filed patent application, which the USPTO examiners considered to have effectively taught use of the CRISPR/Cas9 technology in eukaryotic cells. In addition, patent applications filed by Sigma-Aldrich and Toolgen that similarly claim use of CRISPR/Cas9 in eukaryotic cells (both of which filed applications before Broad's application) have likewise recently been rejected as being either non-novel or obvious in view of the prior-filed UC patent application with specific respect to its teachings regarding application of the invention to use in eukaryotic cells.

Consistent with the substantive determinations reached by the USPTO regarding the broad teachings of the UC patent application, UC's corresponding cases covering use of CRISPR/Cas9 in all settings, including in eukaryotic cells, have been advanced to grant or decisions to grant in numerous jurisdictions worldwide, including in the United Kingdom, the nearly 40 other countries that are members of the European Patent Convention, and more recently in other jurisdictions such as Australia, New Zealand, Singapore and China.

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 Dr. Emmanuelle Charpentier. CRISPR Therapeutics is headquartered in Zug, Switzerland, with business offices in London, United Kingdom, and 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 leading company in CRISPR genome engineering 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, including information about obtaining research and commercial licenses as well as collaborations, 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's Forward-Looking Statement

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 intellectual property protection of our technology and therapies, the intellectual property positions of third parties, and the therapeutic value, development, and commercial potential of CRISPR/Cas-9 gene editing technologies 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 under the heading "Risk Factors" in the company's most recent annual report on Form 10-K, 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 Statement

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, express or implied statements regarding the intellectual property position and strategy of Intellia's licensors; and Intellia's ability to advance CRISPR/Cas9 into therapeutic products for severe and life-threatening diseases and its CRISPR/Cas9 intellectual property portfolio. 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 annual report on Form 10-K 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.

CRISPR CONTACTS

Media:
Jennifer Paganelli
WCG for CRISPR
+1 347-658-8290
jpaganelli@wcgworld.com

Investors:
Chris Brinzey
Westwicke Partners for CRISPR
+ 1 339-970-2843
chris.brinzey@westwicke.com

INTELLIA CONTACTS

Media:
Jennifer Mound Smoter
Senior Vice President, External Affairs & Communications
+ 1 857-706-1071
jenn.smoter@intelliatx.com

Investors:
Graeme Bell
Executive Vice President, Chief Financial Officer
+ 1 857-706-1081
graeme.bell@intelliatx.com

CARIBOU CONTACT

Greg Kelley
Feinstein Kean Healthcare
+ 1 404-836-2302
gregory.kelley@fkhealth.com

ERS GENOMICS CONTACTS

MacDougall Biomedical Communications
Mario Brkulj or Dr. Stephanie May
+49 89 2420 9345 or +48 89 2420 9344
mbrkulj@macbiocom.com or smay@macbiocom.com