116TH CONGRESS
1ST SESSION

S. _____

To increase research, education, and treatment for cerebral cavernous malformations.

IN THE SENATE OF THE UNITED STATES

Mr. UDALL (for himself and Mr. HEINRICH) introduced the following bill; which was read twice and referred to the Committee on _____

A BILL

To increase research, education, and treatment for cerebral cavernous malformations.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the ''Cerebral Cavernous Malformations Clinical Awareness, Research, and Education Act of 2019'' or the ''CCM–CARE Act''.

SEC. 2. FINDINGS.

Congress finds as follows:

(1) Cerebral cavernous malformations (referred to in this section as ''CCM''), also known as cav-

ernous angioma, or cavernoma, is a devastating blood vessel disease characterized by vascular lesions that develop and grow within the brain and spinal cord.

(2) Detection of CCM lesions is achieved through costly and specialized medical imaging techniques, often not accessible or convenient to patients who need them.

(3) While CCM is a common type of vascular anomaly, many individuals are not aware they have the disease until the onset of serious clinical symptoms. CCM is often inherited unknowingly.

(4) CCM affects an estimated 600,000 people in the United States.

(5) Individuals diagnosed with CCM may experience neurological deficits, seizure, stroke, or sudden death.

(6) Due to limited research, there is currently no treatment for CCM other than brain and spinal surgery, and only for certain patients.

(7) There is also a shortage of trained physicians to provide skilled and timely diagnosis and appropriate treatment for CCM.

(8) While the hereditary form of CCM may occur among any ethnicity, the presence of a muta-

tion called the ''common Hispanic mutation'', has passed through 14 or more generations of American descendants from the original Spanish settlers of the Southwest in the 1590s. New Mexico has the highest population density of CCM in the world; Texas, Arizona, and Colorado also have high rates of CCM due to the common Hispanic mutation.

(9) A second mutation (CCM2 Common Deletion) originating in the Southeastern United States before 1800 has increased rates of the illness in South Carolina, Georgia, Florida, Alabama, Mississippi, Louisiana, Texas, Oklahoma, Kentucky, Kansas, and northern California.

SEC. 3. EXPANSION AND COORDINATION OF ACTIVITIES OF NATIONAL INSTITUTES OF HEALTH WITH RESPECT TO CEREBRAL CAVERNOUS MALFORMATIONS RESEARCH.

Part B of title IV of the Public Health Service Act (42 U.S.C. 284 et seq.) is amended by adding at the end the following:

''SEC. 409K. CEREBRAL CAVERNOUS MALFORMATIONS RESEARCH ACTIVITIES.

''(a) EXPANSION AND COORDINATION OF ACTIVITIES.—The Director of NIH, in coordination with the directors of the National Institute of Neurological Disorders

and Stroke, the National Center for Advancing Translational Sciences, the National Heart, Lung, and Blood Institute, and other national research institutes, as appropriate, for the purpose of conducting research and related activities concerning cerebral cavernous malformations (referred to in this section as 'CCM')—

''(1) shall strengthen and coordinate efforts of the National Institutes of Health; and

''(2) may award grants and cooperative agreements to public or nonprofit private entities (including State health departments, political subdivisions of States, universities, and other medical or educational entities).

''(b) ACTIVITIES.—The research and related activities described in subsection (a) shall include the following:

''(1) CLINICAL, TRANSLATIONAL, AND BASIC RESEARCH.—The Director of NIH shall conduct or support, through funding opportunity announcements, grants, or cooperative agreements, basic, clinical, and translational research on CCM, including research on—

''(A) the identification and development of biomarkers that fulfill the requirement of the Food and Drug Administration for biomarker qualification as proper measures of CCM patho-

genic biology or response to clinical intervention;

"(B) safety or efficacy for new or repurposed currently approved drugs for CCM treatment;

"(C) research related to improving and measuring the quality of life for individuals with CCM and their families;

"(D) contributions of genetic variation to clinical presentation as targets for therapy;

"(E) early detection, diagnosis, and treatment of CCM;

"(F) clinical training programs aimed at increasing the number of scientists and clinicians who are trained to treat patients and carry out the research described in this paragraph;

"(G) continued development and expansion of novel animal models for preclinical research relating to CCM;

"(H) pre-clinical and clinical research related to repurposing currently approved drugs for CCM treatment;

"(I) proteomic, pharmacological, and cell biological analysis of CCM molecules;

"(J) biological mechanisms for lesion genesis, development, and maturation;

"(K) biological mechanisms for lesion bleeding and symptomology;

"(L) novel biomedical and pharmacological interventions designed to inhibit new lesion development, lesion growth, and lesion bleeding;

"(M) novel biomedical and pharmacological interventions designed to target existing lesions to reduce their size and clinical activity;

"(N) continued research related to understanding better the natural history and clinical variation associated with CCM, particularly as it relates to the development of drug development tools and clinical outcome assessments;

"(O) the gut-brain axis and the effects of microbiome composition on clinical symptomology; and

"(P) the microbiome as a therapeutic target for CCM treatment.

"(2) FACILITATION OF RESEARCH RESOURCES; CLINICAL TRIAL PREPAREDNESS.—

"(A) IN GENERAL.—The Director of NIH shall award grants and contracts to public or nonprofit private entities to fund all or part of

the cost of planning, establishing, and providing basic operating support for a network of CCM Clinical Research Centers, including Coordinating and Participating centers regarding research on various forms of CCM.

''(B) CLINICAL AND RESEARCH COORDINATION CENTERS.—

''(i) IN GENERAL.—The Director of NIH shall build upon the network created by the U01 Clinical Trial Readiness Research Project to identify and support the development of 2 geographically distributed national clinical and research coordinating centers with unique clinical expertise and the potential for coordinating multi-site clinical drug trials with respect to CCM.

''(ii) DUTIES.—The coordinating centers identified under clause (i) shall provide a model for the participation centers described in paragraph (3), facilitate medical research to develop a cure for CCM, and enhance the medical care of individuals with CCM nationwide, including by—

''(I) maintaining an institutional infrastructure capable of hosting clin-

ical trials and facilitating translational research projects and collaborations for clinical trials;

''(II) implementing the programs dedicated to patient education, patient outreach, and awareness developed by the Cerebral Cavernous Malformations Consortium under subsection (c)(3)(B);

''(III) developing the capacity to establish and maintain communication with other major CCM research and care institutions internationally for information sharing and coordination of research activities;

''(IV) demonstrating clinical expertise in the management of CCM and appointing a director and support staff, including a trainee and patient representative, for CCM research programming;

''(V) treating a sufficient number of eligible patients for participation with particular focus on unique subpopulations, such as patients with the

common Hispanic mutation, Ashkenazi Jewish mutation, CCM2 Common Deletion, or CCM3 gene mutation carriers; and

"(VI) maintaining a telehealth infrastructure to support and provide clinical consultation for remote and underserved communities.

"(3) PARTICIPATION CENTERS.—

"(A) IN GENERAL.—The Director of NIH shall build upon the network created by the U01 Clinical Trial Readiness Research Project to identify and support the development of approximately 6 to 10 clinical and research participation centers to facilitate medical research to develop a cure for CCM and enhance the medical care of individuals with CCM, in partnership with the coordinating centers under paragraph (2) and other national and international entities, as appropriate.

"(B) ELIGIBILITY.—To qualify for selection as a participation center under subparagraph (A), an entity shall—

"(i) at the time of selection—

''(I) be affiliated with an established research network of the National Institutes of Health; and

''(II) have the potential to participate in a multisite clinical drug trial with respect to CCM;

''(ii) demonstrate—

''(I) an institutional infrastructure capable of hosting a clinical trial site and facilitating translational projects and collaborations for clinical trials;

''(II) the capacity to maintain communication with other major CCM research and care institutions internationally for information sharing and coordination of research activities, especially through health information technology; and

''(III) clinical expertise in CCM management or complete the CCM clinical training program under subsection (c)(4); and

''(iii) have a sufficient number of eligible patients with CCM.

''(C) DURATION OF SUPPORT.—The Director of NIH may provide support for participation centers under this section for a period not to exceed 5 years. The Director of NIH may extend the period of support for a center for 1 or more additional periods, not to exceed an additional 5 years, if the operations of such center have been reviewed by an appropriate technical and scientific peer review group established by the Director of NIH and if such group has recommended to the Director that such period should be extended.

''(c) CEREBRAL CAVERNOUS MALFORMATIONS CONSORTIUM.—

''(1) IN GENERAL.—The Director of NIH shall build upon the network created by the U01 Clinical Trial Readiness Research Project to convene a Cerebral Cavernous Malformations Research Consortium (referred to in this section as the 'consortium').

''(2) MEMBERSHIP.—The consortium—

''(A) shall include representatives of—

''(i) the coordinating centers selected under subsection (b)(2); and

''(ii) at least 1 national CCM patient advocacy organization, which may be an

entity that receives a grant or contract under subsection (b)(2)(A); and

"(B) may include representatives of the National Institutes of Health or the Food and Drug Administration, in an advisory or ex officio role.

"(3) RESPONSIBILITIES.—Through a consensus based decisionmaking model, the consortium shall divide assignments and be responsible for—

"(A) developing and implementing training programs for clinicians and scientists in accordance with paragraph (4);

"(B) developing patient education, outreach, and awareness programs and materials, which may be tailored for specific regional needs at coordinating centers, including—

"(i) a regional multimedia public awareness campaign;

"(ii) patient education materials for distribution by regional physician and surgeon offices;

"(iii) an education program for elementary and secondary school nurses to facilitate early detection and diagnosis of

CCM in areas in which there is a high density of cases of CCM;

"(iv) regular regional patient and family-oriented educational conferences; and

"(v) nationally relevant electronic health teaching and communication tools and a network of professional capacity and patient and family support; and

"(C) preparing a biannual report to Congress, in accordance with paragraph (5).

"(4) TRAINING PROGRAM FOR CLINICIANS AND SCIENTISTS.—

"(A) IN GENERAL.—The consortium, in cooperation with the coordinating centers, shall establish or expand a physician training program, including information and education on advances in the diagnosis and treatment of CCM, and training and continuing education through programs for scientists, physicians, medical students, and other health professionals and care coordinators who provide care for patients with CCM, telehealth, and research relevant to CCM, for the purpose of supporting the development of new participation centers

through educational programming to gain the expertise needed to become clinical and research participation centers with the potential to participate in clinical drug trials.

''(B) STIPENDS.—The Director of NIH may provide stipends for health professionals who are enrolled in the training programs described in subparagraph (A).

''(C) ELIGIBILITY.—To be eligible to participate in the training program, an individual shall be affiliated with an entity that is in an existing clinical research network of the National Institutes of Health.

''(5) REPORT TO CONGRESS.—The consortium shall biennially submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report that describes the research, education, and other activities on CCM conducted or supported through the Department of Health and Human Services. Each such report shall include—

''(A) a research plan;

''(B) provisions specifying the amounts expended by the Department of Health and

Human Services with respect to various forms of CCM, including those affected by the common Hispanic Mutation, Ashkenazi Jewish mutation, CCM2 Common Deletion, CCM3 gene mutations, and other familial and sporadic forms of cerebral cavernous malformation; and

''(C) recommendations for particular projects or types of projects that the national research institutes or other entities in the field of research should conduct on inherited or non-inherited forms of CCM.

''(d) PRIORITIZE CCM FUNDING FOR BIOTECH.—The Director of NIH, in coordination with the directors of the National Institute of Neurological Disorders and Stroke, the National Center for Advancing Translational Sciences, the National Heart, Lung, and Blood Institute, and other national research institutes, as appropriate, shall prioritize the provision of grant funding for small biotechnology entities that are working to develop treatments for CCM.''.

SEC. 4. CENTERS FOR DISEASE CONTROL AND PREVENTION CEREBRAL CAVERNOUS MALFORMATIONS SURVEILLANCE AND RESEARCH PROGRAMS.

Part B of title III of the Public Health Service Act (42 U.S.C. 243 et seq.) is amended by inserting after section 317T the following:

"SEC. 317U. CEREBRAL CAVERNOUS MALFORMATIONS SURVEILLANCE AND RESEARCH PROGRAMS.

''(a) IN GENERAL.—The Secretary, acting through the Director of the Centers for Disease Control and Prevention, may award grants in such sums as may be necessary and cooperative agreements to public or nonprofit private entities (including State health departments, political subdivisions of States, universities, and other medical or educational entities) for the collection, analysis, and reporting of data on cerebral cavernous malformations (referred to in this section as 'CCM').

''(b) NATIONAL CEREBRAL CAVERNOUS MALFORMATIONS EPIDEMIOLOGY PROGRAM.—The Secretary shall award grants and cooperative agreements, including technical assistance, to public or nonprofit private entities for—

''(1) the collection, analysis, and reporting of data on CCM; and

''(2) epidemiological activities, including encouraging consistency in ICD-10 coding, collecting and analyzing information on the number, incidence, correlates, and symptoms of cases and the clinical utility of specific practice patterns.

''(c) NATIONAL SURVEILLANCE PROGRAM.—The Secretary shall—

''(1) provide for a national surveillance program for the purpose of carrying out epidemiological activities regarding CCM, including collecting and analyzing information on the number, incidence, correlates, and symptoms of cases of CCM and the clinical utility (including costs and benefits) of specific practice patterns; and

''(2) wherever possible, ensure that the surveillance program is coordinated with the data and sample collection activities of the National Institutes of Health under section 409K.

''(d) TECHNICAL ASSISTANCE.—In making awards under this section, the Secretary may provide direct technical assistance, including personnel support.

''(e) COORDINATION WITH CLINICAL CENTERS.—The Secretary shall ensure that epidemiological information is made available to clinical centers as supported by

the Director of the National Institutes of Health under section 409K.

''(f) AUTHORIZATION OF APPROPRIATIONS.—There are authorized to be appropriated such sums as may be necessary to carry out this section.''.

SEC. 5. FOOD AND DRUG ADMINISTRATION CEREBRAL CAVERNOUS MALFORMATIONS CLINICAL TRIAL PREPAREDNESS AND SUPPORT PROGRAM.

(a) BIOMARKER QUALIFICATION PROGRAM.—The Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall coordinate with clinical centers, investigators, and advocates to support the qualification of appropriate surrogate biomarkers in an effort to hasten the pace of clinical trials for cerebral cavernous malformation.

(b) CLINICAL OUTCOME ASSESSMENT QUALIFICATION.—The Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall coordinate with clinical centers, investigators, and advocates to support the qualification of newly developed patient reported outcome measures for quality of life as a clinical outcome in an effort to hasten the pace of clinical trials for cerebral cavernous malformation.

(c) INVESTIGATIONAL NEW DRUG APPLICATION.—The Secretary of Health and Human Services, acting

through the Commissioner of Food and Drugs, shall coordinate with clinical centers, investigators, and advocates to support appropriate investigational new drug applications under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) in an effort to hasten the pace of clinical trials for cerebral cavernous malformation.

(d) ADAPTIVE TRIAL DESIGN AND EXPEDITED REVIEW PATHWAYS.—The Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall coordinate with clinical centers, investigators, and advocates to support appropriate adaptive trial designs for rare disease research and expedited peer review mechanisms for including Orphan Drug Designation, Fast Track, Breakthrough Therapy Designation, Priority Review or Accelerated Review, where appropriate, in an effort to hasten the pace of clinical trials for cerebral cavernous malformation.