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Clinical research in OA – the NIH Osteoarthritis Initiative

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Scientific and clinical experts in the field of osteoarthritis currently perceive that the lack of discreet indicators of disease progression that are acceptable to the U.S. Food and Drug Administration (FDA) as clinical endpoints is a major obstacle to the ability to diagnose, monitor, and treat this degenerative joint disease. The largest public-private partnership on knee osteoarthritis underway at the NIH, the Osteoarthritis Initiative (OAI), was launched in 2002 by the NIH and the FNIH as an innovative collaboration to develop a public research resource for the identification of new biomarkers and treatment targets for knee osteoarthritis. An overarching goal is to create a public resource to validate prospective biomarkers of disease onset and progression, obtain early-stage input from the FDA as to the acceptability of biomarkers as clinical endpoints, and ensure that validated biomarkers are as widely available as possible to further product development and the public health. Additional goals were to determine whether information obtained from serial magnetic resonance imaging (MRI) of the knee would provide more sensitive indicators of onset and progression of osteoarthritis. Additionally, biological specimens have been collected that, in combination with the clinical and imaging data, could be used for validation of single or combination biochemical markers as indices of various aspects of disease.

This 4-year longitudinal study is following 4,800 participants with either established osteoarthritis of the knee (~1,300) or significant risk factors for the development of osteoarthritis of the knee (~3,500) to produce a public resource database of imaging and clinical data to help identify and characterize the disease from onset to joint replacement. There are currently data and images available for the baseline, 12- and 24-month visits of the cohort. Data from the 36-month visit will be available in the coming year. The cohort is 58% female with 21% minority enrollment. There are three sub-groups: progression (29%), incidence (68%), and non-exposed (3%). The ages ranged from 45-79 at baseline and the distribution of ages ranges from 12% in the youngest to 23% in the oldest with 30% in the middle years. Biospecimens (blood and urine) are obtained at every visit and DNA has been extracted from all the baseline specimens. These specimens are available by application.

The OAI clinics began the fourth and final year (in the existing contract) of follow-up visits for the cohort in 2008. The NIH and other consortium members have determined that widespread availability of validated biomarkers and other research tools arising from use of the OAI resource by third parties is necessary to maximize the public health benefit of the Initiative. Thus, renewable resources from the OAI, such as clinical data and X-ray information, are made freely available to qualified scientists everywhere. These clinical and imaging data have been released to the OAI public web site (http://www.oai.ucsf.edu) at regular intervals since June 2006. Currently there are over 850 registered users of this public web site in 47 countries. Over 1,500 clinical data sets have been downloaded and 87 image data sets have been distributed to national and international users. For OAI resources that are limited, such as the biospecimens, priority will be given to the validation of biomarkers that, in addition to demonstrating scientific merit, will be made widely available for use in accordance with the NIH Principles and Guidelines on Obtaining and Disseminating Biomedical Research Resources.

The OAI relies on the following clinical centers and their principal investigators: University of Maryland School of Medicine, Baltimore: Marc Hochberg, M.D., M.P.H.; The Ohio State University, Columbus: Rebecca Jackson, M.D.; University of Pittsburgh: C. Kent Kwoh, M.D.; Memorial

The author has no conflict of interest.

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Hospital of Rhode Island, Pawtucket: Charles Eaton, M.D. and is led by Michael Nevitt, Ph.D., Principal Investigator of the data coordinating center at the University of California, San Francisco. A Steering Committee advises on the scientific aspects of the study. The National Institutes of Arthritis and Musculoskeletal and Skin Diseases and the National Institute on Aging lead this initiative and are joined by the National Center for Complementary and Alternative Medicine, the Office of Research on Women's Health, the National Institute for Dental and Craniofacial Research, the National Center for Minority Health and Health Disparities, and the National Institute for Biomedical Imaging and Bioengineering to provide the federal support for this initiative. The Foundation for NIH organized and oversees the private-sector partners that include GlaxoSmithKline, Merck, Novartis, and Pfizer. The FDA participates in this initiative in an advisor manner.