**Response of Bruce W. Stillman to Office of Science and Technology Policy Request for Information re: Building a 21st-Century Bioeconomy**

I welcome the Administration's announcement of its intention to draft a National Bioeconomy Blueprint, and wish to submit several "grand challenge" suggestions, as requested by OSTP.

**1. Launch a national Cancer Therapeutics Initiative**

There is an outstanding opportunity to apply recent scientific and technological advances to the development of new classes of anti-cancer drugs and diagnostics, and do so much more rapidly and cost-effectively than has been possible heretofore. Such an Initiative would leverage information gleaned from the National Cancer Institute's Cancer Genome Atlas project, and would move beyond it in important ways to rapidly transform recent basic science discoveries into targeted therapies that address the disease's genetic and epigenetic diversity.

Comprehensive knowledge of mutated cancer genes in major tumor types will not in itself enable us to halt cancer. Using revolutionary RNA interference-based screens, we now, however, have the ability to identify the Achilles' heels of tumors in an unbiased fashion; this enables us to discover factors of all kinds, and not just those with gene mutations, that drive cancers in patients. These factors, including a plethora of cellular proteins with no previously known connection to oncogenesis, constitute an entirely new pool of potential drug targets. Especially exciting is the fact that we now possess the tools, notably animal models, with which to validate these targets in a preclinical setting that closely reflects the human clinical experience. A second phase of the Initiative would focus on discovering drugs against the new targets and testing them in the same model systems. Because these models are based on human cancers, this should significantly increase the probability of clinical success. Furthermore, by identifying patient-specific targets and drugs during pre-clinical testing, this system is likely to reduce costs by requiring far fewer patients to be enrolled in trials. This Initiative has the prospect of generating targeted, non-toxic therapies against a broad range of cancer types and subtypes over the next decade, including those we have had little success in treating such as cancers of the blood, brain, lung, prostate, ovaries, pancreas and liver.

**2. Make a major commitment to fundamental neuroscience**

As vividly documented by the National Institute of Mental Health, the costs of mental illness in the United States are extraordinary. Quite apart from the impact upon national productivity there is the incalculable human cost to victims and those who love and care for them, often over periods spanning decades. We need to make a major investment in basic research in neuroscience and related fields because, to be frank, they are *one to two decades behind* the state-of-the-art in fields now at the forefront of biological discovery, most notably cancer research. We are in a position to achieve the objectives of the cancer initiative sketched out above precisely because our basic understanding of cancer and related cell biology and genetics has advanced so far, especially since the completion of the Human Genome Project. Our near-term (5-to-10-year) aim in a basic science initiative in neuroscience should be to attain a much more detailed understanding than we

presently have of the biological correlates of cognitive dysfunction, and in particular, knowledge of the neural networks and cellular and intracellular pathways causally involved in major disability-causing mental illnesses including autism, schizophrenia, depression, and the family of stress- and anxiety-related disorders including post-traumatic stress disorder. The near-term fruits of acquiring such understanding likely will be our first reliable and objective non-invasive diagnostics for common mental illnesses and much better quantitative measures of these illnesses, which will help pave the way toward new treatments.

**3. Invest in basic plant science, to address energy and food needs**

Our fundamental knowledge of plant life, like that of the workings of the brain, is lagging. Our federal government should commit to the grand challenge of significantly increasing funding for basic plant science, with the specific aim of generating the knowledge we need to produce commercially viable biofuels and to increase yields of food crops. We have made some progress on biofuels in recent years, but still lack fundamental knowledge that has the potential to transform the efficiency, and therefore economics, of biofuel production. Basic research is needed to increase the photosynthetic efficiency of plants and algae to optimize the use of available sunlight in converting light into carbon. Complementary basic research is needed to determine how to convert the fixed carbon into lipid and oil and store that oil in vesicles before harvesting for biofuel. At the same time, with the global population recently having passed the 7 billion mark – on its way perhaps to 9 or 10 billion – we should be neither naïve nor complacent about future food needs. The United States should be at the forefront of applied research in plant science, but can only achieve this if we significantly increase funding right now in basic plant science.

**4. Continue to invest in the training of scientists**

Our federal government must not fail to invest in training the next generation of scientists if The United States is to remain at the cutting edge. All of the initiatives and investments outlined above are predicated upon the assumption that we will continue to be a magnet for the finest young people who choose to devote their talents to advancing scientific knowledge. With cutbacks looming in NIH funding, training programs are often the first things eliminated. We must make certain that this does not happen, or risk losing our preeminent status in the sciences.

**5. "Applied science" goals must not be pursued at the expense of basic research**

The initiatives and efforts outlined above each depend upon continued robust funding of basic science. Grand challenges can help clarify our priorities, and applications of new knowledge must be vigorously pursued. But *we must not do so at the expense of basic research*. All that we accomplish in applied science, from developing more effective cancer treatments to inventing new biofuels and crops that will adjust to climate change, is possible because of advances we have made in fundamental biological understanding. Such advances, like the discovery of RNA interference, cannot be predicted. But we can say with confidence that they cannot and do not occur absent robust investments in basic science and in the training of new scientists and members of the technology workforce. A vivid example of how such investments pay off is the Human Genome Project, which not

only gave rise to the novel field of genomics, but also, as the Battelle Memorial Institute has estimated, generated $796 billion in direct and indirect economic activity within the first decade since its completion. This includes some $244 billion in personal income and an impressive 3.8 million job-years of employment.[1] Considering the federal government's investment of $3.8 billion in the HGP through 2003 (less than $6 billion in current dollars, and an amount now recouped *annually* in genomics-related taxation alone) the return on investment has been $141 for every $1 invested. This investment in basic science – made without a guaranteed practical benefit – has not only been the single most influential investment made in modern science, but must rank as one of the wisest ever made in any American undertaking.

**6. A cautionary word: Against institutionalization**

In funding major scientific initiatives we must take pains not to establish infrastructures that become permanent. It would be a mistake, in our view, to institutionalize grand challenges. Each that is undertaken should be pre-planned to have a ramp-up and ramp-down phase. It is also vital that each initiative be peer-reviewed, to insure both the integrity and appropriateness of the investments that are made.

Sincerely,

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President
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[1] Battelle Memorial Institute, "Economic Impact of the Human Genome Project," May 2011, p. ES-2.