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COGR Response to NIH on Discovering New Therapeutic Uses for Existing Molecules

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an organization of research universities

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National Institutes of Health
Department of Health & Human Services
Attention: NOT-TR-12-002
[Submitted electronically at
http://grants.nih.gov/grants/rfi/therapeutics_discovery/index.cfm?ID=24]

Re: NOT-TR-12-002 / Request for Information (RFI): Input on the NIH-Industry Program to Discover New Therapeutic Uses for Existing Molecules

Dear Sir or Madam:

This is in response to the NIH/NCATS RFI for Input on the NIH-Industry Program, Discovering New Therapeutic Uses for Existing Molecules (NOT-TR-12-002). The Council on Governmental Relations (COGR) is an association of more than 185 U.S. research universities and their affiliated academic medical centers and research institutes. COGR concerns itself with the impact of federal regulations, policies, and practices on the performance of research and other sponsored activities conducted at its member institutions.

We appreciate the opportunities and challenges inherent in this new and highly visible NIH initiative. Our member institutions and their researchers look forward to partnering with NIH/NCATS to advance therapeutics development through drug rescue and repurposing activities supported by the new program.

Our member institutions have considerable experience working with pharma and biotech companies, including the three companies that are participating in the pilot. In fact, a number of our institutions have template agreements in place with such companies. While template agreements can reduce transaction costs, it is vitally important that they contain terms acceptable to all parties. We note that while the university community was represented in the NIH-Industry Roundtable mentioned under "Background" in the RFI, to our knowledge university representatives were not invited to participate in the actual development and negotiation of these templates.

As an overall comment, the companies are providing drugs but not funding, yet the terms NCATS has presented in the templates go beyond what academic institutions typically agree to for investigator-initiated studies that are fully funded by a company. Some of these terms are likely to present significant problems for

our institutions. Moreover, it appears that federal officials have negotiated these templates “on behalf” of the academic community, which places the recipient institutions in a difficult position when negotiating institution-specific requirements. We believe it is relatively unprecedented for federal agencies to prenegotiate the terms of contracts between two private entities. While it is certainly appropriate for the NIH to point out where provisions in the contracts must be consistent with the requirements of federal funding, we are deeply concerned that NIH’s involvement in negotiating terms such as those related to indemnification, compensation for subject harm, or details of publication is an unwarranted intrusion into the rights of universities and research organizations to manage such matters themselves.

The subject RFI requests (#2) comments on how the current Confidential Disclosure Agreements (CDAS) and Collaborative Research Agreements (CRAs) might affect participation in the program. Unfortunately there are a number of provisions in the CRAs that in our view may be potential “deal breakers” for many of our institutions. We discuss these issues in more detail below, but we want to single out several in particular. One is the broad scope of rights to “Technical Developments” which is common to the CRAs with all three participating companies. These rights are overly broad, and not likely to be acceptable to many COGR members. Another is the Indemnification provisions in all three agreements. Acceptability of indemnification provisions is highly institution-specific, particularly for public institutions, and does not easily lend itself to a template approach. In some cases, state laws or board of trustee policies may strictly limit indemnity for specific institutions. While we have identified some specific issues with the Indemnification terms in the CRAs, institutions may have additional concerns with the terms that will prevent them from agreeing to them. Other provisions that potentially are very problematic include those on the ownership of intellectual property, publication, and choice of law and jurisdiction. Finally, for a program that has a stated intent to quickly move compounds into the clinic, the agreements are oddly devoid of necessary terms related to representation that compounds will be manufactured and labeled to cGMP standards, and that companies will permit appropriate cross-reference of their Master Drug Files.

Below are our detailed comments on the terms in the template agreements. Given that our focus is on the templates, we are not providing responses to the other issues for which NCATS is seeking responses in the RFI. We have chosen to comment mostly on the potential “deal breaking” provisions that would likely prevent many research universities, especially the publics, from participating in these exciting new NCATS programs. We also note a number of other potentially problematic terms.

1. **“Technical Developments”** - All three CRAs define this term as including any invention, discovery, composition, enhancement, technology, advancement, know-how, process, data, device, machine, material, software or any other information arising from the Program (including any such development protectable by patent, copyright, or other protection under the law in which a Party has an ownership interest). The agreements give the company exclusive commercial option rights to such Technical Developments in which a collaborating academic institution has rights and interests and a royalty-free nonexclusive research license.

This definition is overly broad, particularly to the extent it includes non-patentable inventions, know-how and data “arising from” the Program. As worded, it appears to cover raw data and other original source material, and could include data related to the program but collected independently. Non-patentable information such as data and know-how cannot generally be licensed. The broad definition also raises issues regarding student theses, faculty publications, etc. The license rights should be limited to patentable inventions conceived and reduced to

practice in the direct performance of the study. In particular, exclusive access to unpatentable research results is only possible by withholding the results from publication, which is antithetical to the academic mission of dissemination of new knowledge. To the extent that the language can be read as claiming rights in copyrightable results of the research, this provision could prevent faculty from signing the necessary copyright assignments to have their work published in peer reviewed journals. We have additional concerns about the provision that ownership of technical developments shall be determined according to their “origin” in all three agreements (7.2 Lilly, 8.2 Pfizer and AstraZeneca). This is extremely vague and could lead to assertions that all data and other technical developments originated from the company (since the compound is owned by the company) and are therefore owned by it. This language goes beyond what is reasonable or necessary to protect the companies who are participating in this taxpayer funded program.

2. **Intellectual Property Ownership** - All three CRAs have provisions requiring institutions to have policies and procedures in place to cause all personnel to vest all Technical Developments and Patents created by the personnel in the institution. This requirement again should be limited to patentable inventions. As written it would include vesting of all data, know-how, copyrighted material and other information arising from the Program, which is inconsistent with the policies and practices of most academic institutions and raises serious issues with regard to scholarly publication rights and original data. To the extent that the broad definition of Technical Developments can be viewed to encompass human subject data or samples generated in the course of the research, many institutions may see ethical issues with granting the rights requested to the compound providers.

The terms also require collaborating institutions to grant, at the outset of the project, future rights to both a non-exclusive research license and an option to an exclusive commercial license to their rights in Technical Developments. This creates problems for institutions that need to track the grant of licenses carefully to ensure non-conflicting obligations. It creates a further problem given the scope of “Technical Developments” – it goes beyond the scope of patentable inventions conceived and reduced to practice in the direct performance of the research, making the need to track the grant of these licenses to ensure institutions do not breach their obligations here, or with other parties, such as the federal government. Given that institutions do not typically have rights that the companies seek to the broad spectrum of research results (other than to statutorily protectable intellectual property, and certain narrow categories of other rights), one wonders what such a requirement accomplishes. If the participating companies are primarily concerned that they will be “blocked” from further developing the compounds, this goal could be met by more tailored language, in which the academic partner agrees not to assert certain rights against the participating company.

3. **Indemnification and Representations and Warranties** - Acceptability of indemnification provisions varies widely among institutions, and the terms usually are specific to the institution, especially for public institutions. For this reason they do not lend themselves to a standardized template approach. In the case of these agreements, the carveouts to company liability are too broad, and should apply only “to the extent” the claim arises from the institution’s negligence. In addition, the agreement should provide that the companies cannot admit fault or wrongdoing of the institution without its prior written consent, and that the institution has the right to participate in defense at its own cost and expense. It also would be

advisable to add a provision addressing the company's obligation to compensate for injuries to subjects in the case of company-sponsored protocols. Quite frankly, the determination of the appropriate division of the risks of third party claims between private parties is not a matter that a federal agency should negotiate on behalf of those private parties. In addition, all three agreements contain representations and warranties that go beyond what many institutions can or will agree to for research projects. In particular, the AstraZeneca agreement contains an additional provision for indemnification by the institution from breach of the agreement or any representation or warranty. This is unlikely to be acceptable to most institutions. We question why it is included in this agreement and not the other CRAs.

4. **Publication** - The AstraZeneca and Pfizer CRAs give the companies the right to "revise" manuscripts to ensure protection of the company's confidential information and to delay publication for any invention owned by the institution. It is critical to academic institutions that companies not have the right to "revise;" they should be entitled to review the manuscript for confidential information and the institution should be required to remove any confidential information that may have been included.

5. **Choice of Law** - While the choice of governing law is properly left to individual agreements in the CRAs, in two of the CDAs (Lilly and AstraZeneca) it is subject to the laws of the state of Delaware and the jurisdiction of the federal courts (and state courts in the case of AstraZeneca) for Delaware. This is unlikely to be acceptable to some institutions, especially public institutions, and may raise issues of sovereign immunity.

The following provisions also are problematic, but may be less likely to affect the willingness of institutions to participate in the Program.

6. **"Confidential Information"** - The CDAs vary in their definition but all provide that the definition includes information marked or declared by the company to be confidential. However the Lilly agreement specifies that "confidential information" also includes information about the "discovery, development and properties of compounds to be discussed, as well as clinical trial design and execution." All three CDAs should limit the definition of "Confidential Information" to include the information as specified in the Eli Lilly agreement, and be further limited to include only that information which the company provides to the institution for the purpose of evaluating whether to conduct a study with the company's compound. A core value of academic institutions is the ability to freely disseminate information; exceptions should depend on the purpose and nature of information provided, rather than a third party designation.

The CRAs also vary in their definition. Two (Lilly and Pfizer, 2.6) include the concept of know-how or other information communicated by the company. The other (Astra Zeneca) does not specifically include know-how, but expansively defines the covered information. These definitions are too broad. To the extent data, notes, etc. are included they raise issues of openness and the ability to publish research findings, notwithstanding the acknowledgment of the importance of publication in the CRAs. The CRA definition should be clearly limited to proprietary information embodying the company's technology, processes, business information or objectives. In addition, all three agreements provide that their terms and conditions shall be considered confidential. This may pose a problem for public institutions, which may be required

to disclose agreement terms pursuant to state public or open records laws and whose routine practices do not accommodate the treatment of a research agreement as confidential.

Finally, the CDAs do not reference the CRAs, all of which address Confidentiality. The terms of the CDAs are two years, with varying terms for the termination of the receiving party's obligations (three years in the case of Pfizer and Lilly; five years in Astra Zeneca). This leaves ambiguous which agreement governs once a CRA is entered into. We believe the CRA provisions should supersede the CDA, and the agreements should so state.

7. **Patent Prosecution for Joint Inventions** - Normally institutions prefer to take the lead in the patent prosecution process, including with regard to responding to opposition and other proceedings. This may become even more important with the implementation of the America Invents Act with its provisions for supplemental examinations, post grant review, etc. Yet the agreements give the companies sole responsibility for these actions (Lilly 7.6.1; Pfizer and AstraZeneca 8.6.1). We suggest that institutions should have at least the right of consultation in these matters and that the companies give good faith consideration to university input. At a minimum, this should include a robust right to review and comment not only on the initial drafting of the patent application but also on responses to questions raised during patent examination, approval of claims abandonment, etc. If nothing else, this gives the academic institution the ability to preserve its interests should the company abandon the application later.

8. **Option Periods and Pricing** - We note that these vary among the CRAs. For the most part these terms, with the provisions for designation of Senior Negotiators and arbitration in the case of failure to reach agreement, appear reasonable. However, in the Astra Zeneca agreement, for institution inventions where the company does not obtain an exclusive license, the institution may never offer anyone else more favorable terms (9.2.4). This should be time-limited e.g. 6 months.

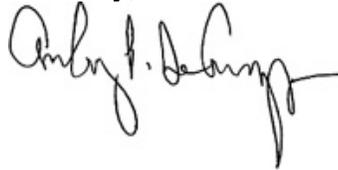
Another issue unique to the AstraZeneca CRA is the pricing provisions (9.2.2). Inclusion of prenegotiated royalty terms in research agreements is problematic for universities, and raises potential tax and other issues. These terms should be deleted.

9. **IIR Agreement** - The CRAs reference an "IIR Agreement" which will be entered into should the parties conduct a clinical trial. They state that the IIR Agreement will be in the "form set out in Exhibit B", yet no terms are included in Exhibit B. Obviously these terms should be made available if the intent is that they also are to provide a template. At a minimum, such an agreement must contain appropriate language regarding: cGMP manufacture of materials provided by industry, rights to cross reference the industry partner's Drug Master File, and compensation for subject harm resulting from the trial.

Given the intent of this program is for NCATS to fund academic institutions to partner with companies, it is vitally important that template agreements reflect the input of all participants. If in the future NCATS plans to develop additional templates of this kind, we urge NCATS to include university representatives in the discussions. Higher ed. institution associations such as COGR, AAMC and others provide a mechanism to broadly reach academic institutions. NCATS may wish to consider this in developing future programs.

We appreciate the opportunity to comment.

Sincerely,

A handwritten signature in black ink, appearing to read "Anthony P. DeCrappeo". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Anthony P. DeCrappeo