Written Testimony of Mr. Dan Larson
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Summary:

This testimony highlights the unprecedented scientific momentum achieved in the field of Polycystic Kidney Disease (PKD) research through technological innovation, cutting edge science and collaboration between private entities and the National Institutes of Health (NIH). PKD research can serve as a model for the NIH to follow when setting standards to find treatments or cures for other serious, life threatening diseases.

Good morning, Mr. Chairman and members of the Subcommittee. My name is Dan Larson, President and CEO of the PKD (Polycystic Kidney Disease) Foundation.

I've been privileged to serve in this capacity since 1993, the year I began lobbying Congress on behalf of nearly 1,400 PKD constituents in each of America's 435 Congressional Districts.

When talking with policy makers over the years about National Institutes of Health (NIH) funding for PKD research, I have continually heard a mixed message. On one hand, there is "the NIH generally knows best" mentality about spending money appropriated to them. On the other hand, there is a sense of frustration that the $29 billion now annually spent on NIH research initiatives has generated too few treatments or cures. This sentiment is growing more and more pronounced.

In this context, arguably one of the best demonstrations of a strong "return on investment" is the field of PKD research. In only 10 years, PKD research has progressed from finding the PKD genes to promising clinical drug trials in humans.

The PKD Foundation has "pushed the envelope" to create unique public and industry partnerships to stimulate PKD research. Add to that effort the passion and generosity of PKD patients and their families, and it is easy to see why private research funding for PKD has increased more than 400 percent in seven years.

In addition, PKD families across the nation have become more engaged in grass roots advocacy efforts. Their efforts, along with the unprecedented scientific momentum currently underway in PKD research, have prompted Congress to adopt increasingly supportive Congressional Appropriations report language for PKD for 16 consecutive years.

This report language, in turn, has prompted the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to establish PKD Centers of Excellence and issue special RFAs and Program Project Announcements, and conduct several International PKD Strategic Planning Meetings.

The NIDDK's efforts have led to the development of innovative imaging technology for PKD – called CRISP (Consortium for Radiological Imaging Studies in Polycystic Kidney Disease) – that is so accurate and sensitive it reduces by 24 times the number of participants needed for clinical drug trials. The NIDDK also has been a leader in establishing the HALT-PKD clinical trials network, a research project jointly funded by the NIH and the PKD Foundation.

Commensurately, research funded by the PKD Foundation has discovered a class of drugs called "V2 receptor antagonists" that may stop a key hormone from causing cyst growth. Research has shown these drugs are highly effective in slowing disease progression in laboratory animals with PKD with little or no side effects.

When a drug company published data showing their V2 receptor antagonist drug impacts other fluid retention diseases in humans, the PKD Foundation immediately began a collaborative relationship with the company to help recruit patients and medical advisors for their 2006

worldwide Phase III clinical trials. This is an effort the PKD Foundation is now duplicating with other drug companies.

These developments have aided in the Food and Drug Administration granting its "Fast Track" designation to the V2 receptor antagonist drug to speed up its development and review.

Let me stress that I am not here today to say the PKD Foundation is the "gold standard" of funding promising research or in working in partnership with other private and public entities. Rather, my intention in citing the above examples of progress is to show that PKD research is as a clear example of how a small NIH grants portfolio (compared to that of other, much less prevalent diseases) can generate therapies for millions of PKD sufferers; save billons of Federal Medicare and Medicaid dollars from kidney failure caused by PKD; and free up 3,000 to 5,000 spots on the kidney transplant waiting list.

I hasten to add, however, that if redirecting NIH resources toward such promising areas of scientific momentum and therapeutic opportunity are not developed, then promising therapies for PKD will be in jeopardy.

Finally, as Congressional Committees take up legislation reauthorizing the NIH in the coming months, I sincerely hope a set of objective priority setting standards will be adopted that account for disease prevalence; morbidity, mortality, cost to the Federal government; scientific momentum; private/public/industry "teamwork;" therapeutic opportunity; and collateral benefits to other research efforts like PKD.

Make no mistake that this effort is vitally important for hundreds of thousands individuals with PKD, including Heidi Cambareri from Westchester County, New York. PKD has threatened the lives of every generation of her New York family. Her grandfather and great-grandmother died from the disease, and her father was forced to rely on a transplant to live. Heidi's sister also has PKD, and now Heidi, too, has the disease. Her hope is that a treatment or cure will be found before her two daughters, ages 2 and 4, are tested or diagnosed.

Dr. Jared Grantham, a world renowned researcher at the University of Kansas Medical Center and the "Godfather" of PKD research, perhaps summed up it best when he wrote: "Humans almost hold sacred the genes they transmit to their descendants. When mistakes that cause distress happen in those genes, great passion is released within and about the family. The PKD community has been able to harness some of the energy of that passion and direct it to a constructive end point."

Thank you – and I'd be happy to answer any questions you may have.

Facts about Polycystic Kidney Disease (PKD)

More than 600,000 Americans and 12.5 million newborns, children and adults worldwide battle PKD each and every day.

PKD is the most common of all life-threatening genetic diseases, affecting more people than Down syndrome, cystic fibrosis, muscular dystrophy, hemophilia, sickle cell anemia and Huntington's disease, combined.

There is no treatment or cure for PKD. Until one is found, PKD will threaten the lives of every generation of every family living with the disease.

PKD equally affects men, women and children regardless of age, race, geography or ethnic origin. It does not skip a generation.

This often-devastating disease comes in two hereditary forms: autosomal dominant polycystic kidney disease (ADPKD), the more common of the two, and autosomal recessive polycystic kidney disease (ARPKD), a relatively rare disease that often causes significant mortality in the first month of life.

Parents with the dominant form of PKD have a 50 percent chance of passing the disease on to each of their children.

Those who do inherit PKD develop fluid-filled cysts on both kidneys. Over time, these cysts grow and multiply, causing the kidney to increase sometimes dramatically is size. Although a normal kidney is roughly the size of a human fist, PKD kidneys can grow to be the size of a football or larger and weigh as much as 38 pounds each.

In 2005, the NIH only devoted $35 million for PKD research – despite the fact that PKD costs the federal government more than $2 billion per year through Medicare and Medicaid costs for dialysis, transplantation and related treatments.

Common PKD symptoms include high blood pressure, constant or intermittent pain in the back and side of the stomach, blood in the urine, kidney stones, frequent urinary tract infections and a family history of kidney problems, heart problems or stroke.

More than 60 percent of people with PKD will develop kidney failure and be forced to depend on dialysis or a transplant to live.

PKD Research Update: Clinical Initiatives

The following is a summary of current clinical initiatives in the field of PKD research:

CRISP – Consortium for Radiological Imaging Studies in Polycystic Kidney Disease. This study was recently completed and showed that MRI (magnetic refinance imaging) is an excellent means of monitoring PKD disease progression, thus providing a method by which the effectiveness of future drug therapies can be measured.

HALT-PKD – This NIH study is the first randomized clinical trial in the PKD field evaluating whether ACE inhibitors or a combination of ACE and Angiotensin Receptor Blocker (ARB) drug treatments slow disease progression in PKD.

Tolvaptan/Otsuka Pharmaceutical Clinical Drug Trial – This study is looking at the effectiveness of a "vasopressin antagonist drug to slow PKD progression. Phase II is in the final stages and enrollment has begun for Phase III.

Tufts-New England Medical Center – Dr. Vendana Menon, principal investigator, is beginning a non-invasive study to look at the mechanisms leading to the development of heart disease in PKD patients.

PKD Gene Modifier Mapping Study – Dr. York Pei, a Canadian PKD scientist, is conducting an international observational study to map modifier genes for renal disease progression in type 1 ADPKD

Somatostatin – Dr. Guiesseppe Remuzzi, an Italian researcher, is conducting a clinical trial in humans using Ocreotide, a drug currently available to treat a different clinical condition. Initial and promising results have led to a second, larger clinical trial in Italy. His application for a similar project has been submitted to the PKD Foundation. Through a networking contact the PKD Foundation established, the CEO of Novartis Pharmaceutical (which makes this drug) was personally contacted and is now considering this project.

Promising future clinical trials:

Rapamycin – This compound is currently used as an anti-rejection treatment following transplantation in those patients intolerant of the more commonly used drugs. In a small clinical trial, decreased kidney volume was experienced by ADPKD patients on dialysis who took rapamycin. Researchers are now working with the NIH to develop a clinical trial for PKD patients earlier in the disease process, since this drug is well tolerated by PKD patients, and it has been through Phase I and II trials already.

Active Pass Pharmaceuticals – This clinical study will look at the effectiveness of a chloride channel blocker to slow disease progression in PKD. Researchers initially contacted the PKD Foundation and were directed to well known PKD scientists to provide direction and assistance in the development of this clinical trial.

Biographical Information for Dan Larson

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Disclosure Notification Pursuant to House Rule XI, Clause 2(g)

I, Dan Larson, hereby certify that I, nor the PKD Foundation that I represent, have NOT received any Federal grants, sub-grants, contracts or sub-contracts in the current Fiscal Year or either of the two previous Fiscal Years.