F.M. KIRBY FOUNDATION SOLICITATION EVALUATION FORM

DATE: April 13, 2022 **REQUEST DATE:** April 4, 2022
Last grant acknowledgement: Yes
Program Area: Health

APPLICANT:
Alzheimer's Association
National Office
17th Floor
225 North Michigan Avenue
Chicago, IL 60601-7633

CONTACT: Ms. Laura M. Fruge, Executive Donor Advisor, Relationship Development
PHONE: (202) 638-8666
PAYEE OTHER THAN ADDRESSEE: Alzheimer's Disease and Related Disorders Association, Inc.

AMOUNT REQUESTED: $175,000 **NATURE OF REQUEST:** Toward grant awards for Early-Career Investigators through the International Research Grant Program

GRANT HISTORY

LAST GRANT DATE: 5/3/2021 **LAST GRANT AMOUNT:** $125,000
FYE DATE: 6/30/2021 **AFS DATE:** 10/18/2021

2016	$175,000	4/4/2016	For: New Investigator Research Grants, specifically the Molecular Pathogenesis and Physiology of Alzheimer's (Discovery Science or Basic Disease Understanding) category
2017	$150,000	4/28/2017	For: Support for Early-Career Investigators through the International Research Grant Program
2019	$150,000	4/15/2019	For: Support for Early-Career Investigators through the International Research Grant Program
2020	$125,000	4/29/2020	For: Support for Early-Career Investigators through the International Research Grant Program
2021	$125,000	5/3/2021	For: Support for Early-Career Investigators through the International Research Grant Program

DLK COMMENTS: Before I look forward, I will highlight the work of Gabor Egervari, M.D., Ph.D., who was sponsored by the F. M. Kirby Foundation. Dr. Egervari's work focuses on proteins called histones which help activate genes related to learning and memory. Cells modify histones by attaching a chemical group called an "acetyl" to the histones. Recent studies have shown that dysfunction of this process could lead to brain changes related to Alzheimer's. Dr. Egervari and his team are researching whether problems with the ACSS2 (acetyl-CoA synthetase 2) protein may decrease histone acetylation and lead to learning and memory issues. They are studying the location of ACSS2 in brain tissue from individuals who had Alzheimer's and younger and older adults who died from other causes. In addition, they are using genetically engineered Alzheimer's-like mice to study how ACSS2 and histone acetylation alter the activity of genes related to learning

and memory. Finally, they are tracking disease progression to help understand a common molecular pattern that may underlie healthy histone acetylation as well as histone acetylation during the progress of Alzheimer's.

During their first year of study, Dr. Egervari's team found that lack of ACSS2 in the brain significantly worsened learning and memory impairments in the mice. During the second year of the fellowship, the researchers focused on characterizing the molecular changes that occurred in the hippocampus. Their results identified a specific group of cells within the hippocampus of the mice that undergo other changes because of the lack of ACSS2 and may play a role in the development of learning and memory impairments. The results may establish ACSS2 as a therapeutic target for Alzheimer's disease.

Prior to receiving the request, I had a conversation with Laura Frugé, Executive Donor Advisor, who provided an update on some organizational changes. I'm sharing details because most of the things we discussed were quite relevant but not mentioned in the request. Effective November 1, 2021, the CEO/President roles were split to help with succession planning. Harry Johns retained the title of CEO and Joanne Pike was named President. Joanne has been with AA for five years, first as Chief Program Officer and then Chief Strategy Officer. Prior to AA, she spent 13 years at American Cancer Society. Laura also provided some color on the status of Aduhelm (Biogen's drug to treat Alzheimer's) and the other monoclonal antibody drugs that were approved by the Centers for Medicare and Medicaid Services (CMMS). Biogen announced a 50% price cut (down to $27K) for the drug. CMMS has approved it but only for patients enrolled in clinical trials. Unfortunately, the current constituency of the trials (80-90% white) does not align with the broad constituency of people affected (older Blacks are about twice and Hispanics 1.5 times as likely to have Alzheimer's or other dementias as older whites).

As referenced in the request, Congress has been increasing the National Institutes of Health's (NIH) annual budget for Alzheimer's and other dementia research. It now totals over $3.4 billion, a more than seven-fold increase since 2011. In 2021, the Association committed more than $70 million to accelerate research. It still stands by its national goal of preventing and effectively treating Alzheimer's disease by 2025. The Association's active commitments now total more than $300 million and are funding more than 920 best-of-field projects in 45 countries across the four key outcome areas: Discovery Science, Early Detection, Treatment, and Prevention.

According to their request, the Association has been increasing support for diverse scientists from underrepresented communities (Blacks, Hispanics, American Indians and Alaska Natives; Asians: and Native Hawaiians and other Pacific Islanders). This year's proposal is requesting support for their research grants to promote diversity for early-career scientists. The fellowships support researchers in different stages of their careers from early post-graduate work where researchers are not yet in their first independent faculty position, to clinician scientists who are within ten years of receiving an M.D., D.O., or Ph.D. to early-career investigators who are less than 15 years past their post-doctoral degree or post-residency. The Association also offers grants to investigators who are new to the dementia research field with the goal of providing opportunities to investigators with expertise from outside neurodegenerative research to advance Alzheimer's research. The details on increased support for diverse scientists did not seem particularly specific or robust, in contrast to Children's Hospital's recruitment of interns from a diverse community college, so I suggest we continue with our general support for early-career investigators through the International Research Grant program. I'm not quite sure why we scaled the budget back to $100K for AA, other than an overall desire to trim the health docket. We have already scaled them back from $175K in 2014

down to $125K by 2020. I'd be fine funding the full $125K requested for early-career investigator research.

JJK expressed concern with the Association's fundraising expenses (18% of total expenses) for FY20 and estimated 20% fundraising budget for FY21. As it turns out, 17% of total expenses were for fundraising in FY21. I was interested to see what the return ratio was in terms of fundraising expenditures versus contributions for a few of our larger grantees. I looked at strictly revenue that was fundraising-related (excluding investment returns, etc.). American Red Cross's fundraising expenditures of $165M (for FY21) returned contributions five-fold (totaling $834.9M). JDRF's fundraising expenditures of $34.7M (for FY20) returned contributions 5.6 times over (totaling $194.1M). Alzheimer's Association's fundraising expenditures of $64.1M (for FY21) returned contributions six times over (totaling $384.5M) so they appear right in line with our other grantees. Financial analysis attached.

JJK COMMENTS: Since DLK added her comments, Alzheimer's Association has issued a statement regarding Aduhelm and its limited coverage by Medicare to patients enrolled in clinical trials. Aduhelm is intended to work by targeting the amyloid protein, notorious for forming "plaques" in the brains of Alzheimer's patients. An April 6th article in *NY Times* shed a not-always-flattering light on Alzheimer's Association's push to get coverage from the Center for Medicare and Medicaid Services. For context, the F.D.A. came under criticism for approving, under an accelerated approval pathway, what was touted as a revolutionary therapy, which, in fact, had contradictory scientific results, with one trial cohort not appearing to benefit at all from Aduhelm (the other trial cohort showed "slight" slowing of cognitive decline). More alarmingly, according to the *NY Times* article, "40% of patients on a dosage later approved experience brain swelling or brain bleeding, often mild but sometimes serious."

Aduhelm may very well prove beneficial to Alzheimer's patients once researchers can better understand when it is best deployed and what its most effective dosage is. AA is, in their own words, relentless in their fight for Alzheimer's patients and their families, but in this case, it appeared that they were too quick to call a victory.

While the jury is still out on Aduhelm, there is no disputing the power AA has had in promoting Alzheimer's research and advocating for more federal NIH funding. Helping to increase funding by sevenfold since 2011 is a signal of AA's reach and the growing interest in neuroscience and neurodegeneration.

The early-career investigation program is a strong fit for FMKF medical research grants: it attracts early-career investigators, giving them a chance to prove their hypotheses; it helps build the pipeline of researchers interested in neuroscience and neurodegeneration; and it helps to access the deeper pockets of NIH funding, fueling discoveries. Within our general interest in neuroscience and neurodegeneration, considering the preponderance of Alzheimer's amongst the American population – particularly in Black communities – support for Alzheimer's Association's research remains compelling, even as we seek other places within the docket to trim our budget. Furthermore, given the controversy around Aduhelm, our funding for early-career investigators steers us rather clear of this.

Appreciate the help offered by DLK in interpreting the ratio between fundraising expenses and funds raised. I do note that, like American Cancer Society, revenue from branded community

events – like the Walk to End Alzheimer's – continues its downward trajectory. Still a major source of revenue at a projected $75M, but perhaps not the money in the bank that it once seemed.

I recommend $125K for support for Early-Career Investigators through the International Research Grant Program.

APPLICANT: Alzheimer's Association/National Office

F. M. KIRBY FOUNDATION
Financial Statement Analysis

Grantee Name:	Alzheimer's Association - National	**Date:**	4/6/2022
Prepared By:	DLK		
Grant Request Amt.	$ 175,000	**Type of Financial Report Submitted**	Audit
Budgeted Amt.	$ 100,000	**Period Covered in Financial Report**	6/30/2021
Audit Firm	Grant Thornton		
Opinion	Present fairly	**Date of Report Issuance**	10/18/2021
Basis of Acctg.	GAAP		
Current Ratio (Liquidity Ratio/Working Capital Ratio)	2.34	**Amount of Unrestricted Net Assets (Operating Reserve)**	**$ 212,651 (in thousands)**

Note: Current ratio measures an organization's ability to pay short-term and long-term obligations. The higher the ratio, the more capable the organization is of paying its obligations. A ratio under 1 indicates

Allocation of Functional Expenses	6/30/2021	%	Must Read Financial Statement Notes
A. Program Services	$ 294,281	79%	Ideally program expenses should be at least 70% of budget.
B. Management/ General	$ 15,016	4%	
C. Fundraising	$ 64,052	17%	
D. Total Expenses	$ 373,349	100%	
	(in thousands)		

Comments/ Notes:

FY22 Budget - FY22 is projecting an operating deficit of $46.3M versus a surplus of $32.7M for FY21. Total revenues are budgeted to decrease by $34.8M (9%), with the bulk of the decline occurring in contributed income. All line items, with the exception of special events, are budgeted to decline. Total expenses are budgeted to increase by $44.3M (12%). Program services are budgeted to grow by $28M (10%), with increases in every line item. Supporting services are budgeted for an increase of $16.3M (21%), primarily in fundraising. The request of $175K equates to 2.4% of its foundation relations budget.

FY21 Audit - The Association had an operating surplus of $32.9M for FY21 vs $13.3M for FY20. Total revenues declined slightly, down $3.2M (1%), all in conference registrations. Program services declined by $13.0M (4%), with research spending up $6.5M (10%), care/support/risk reduction down $10.4M (10%), and concern/awareness down $10.2M (9%). Supporting services declined by $9.8M (11%), primarily in fundraising. The Association's total net assets grew by $79.1M. Investments totaled $363.7M as of June 30, 2021, of which $24.5M were endowment-related. The Association received $7.2M in gifts-in-kind and contributed services, of which $2.4M was provided for the medical science research grants review process and the AA International Conference, $3.9M as program expense for volunteer services, $779K as fundraising expenses and $81K of other gifts-in-kind. There were no red flags as a result of my review.

APPLICANT: Alzheimer's Association/National Office

DISPOSITION:

( ) Declination

( ) Hold for review on/about**:**

(xx) Approval for**: $125,000**

(xx) Hold for Board Review

(xx) Insert Information**: For: Support for Early-Career Investigators through the International Research Grant Program**

( ) Other**:**

Initials: JJK Date: 4/13/22

Check #:_____ Date:_____