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AKER BIOMARINE

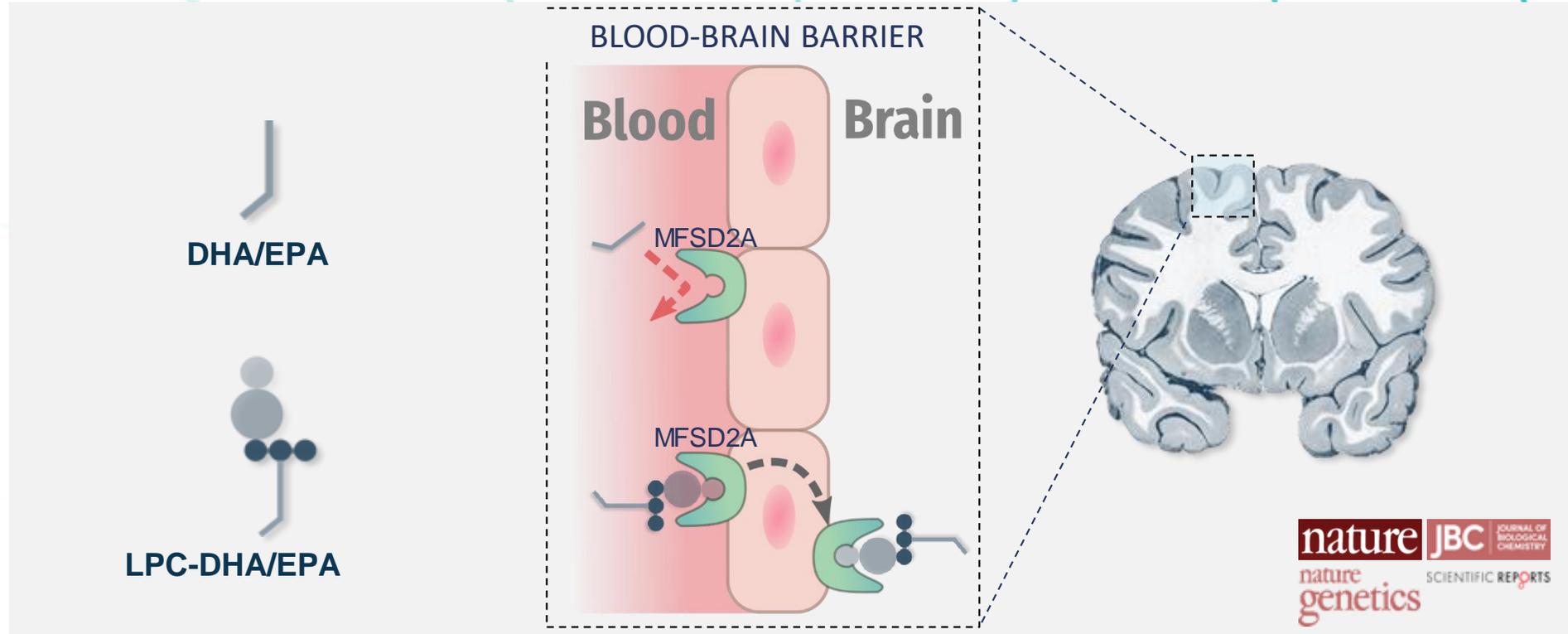
Aker BioMarine and Dr. Michael Davidson enter pharmaceutical collaboration for:

## **Development of pharmaceutical therapies with the use of LYSOVETA - LPC bound EPA/DHA**

Matts Johansen, CEO Aker BioMarine

Michael Davidson, MD, Founder, Medical Food Solutions Research

# LPC, Lysophosphatidylcholine, transports DHA/EPA through Mfsd2a across the selective Blood-BRAIN Barrier



- The brain is protected by the blood-brain barrier
- This barrier is selective and has tight control over which compounds that are allowed to enter into the brain
- Recent studies have established an understanding of how the transport of DHA/EPA into the brain is done in the form of LPC

Aker BioMarine has invested in research, development, IP-rights and commercialization strategies

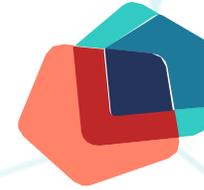
## 6 YEARS OF...

PRODUCT AND PROCESS DEVELOPMENT

RESEARCHING MECHANISMS AND EFFECTS

IN-LICENSING IP

BUILDING COMMERCIALIZATION STRATEGIES



# LYSOVETA

LPC bound EPA/DHA

## STRONG IP PROTECTION IN THE LPC SPACE

Broad IP-protection of production process, raw material and different LPC products, compositions and uses across geographies

### LPC SPECIFIC IP

- 2 granted patents with 21 granted patent claims
- 18 pending applications with 761 patent claims

### OTHER LPC RELEVANT KRILL IP

- 45 granted patents
- 16 pending applications

### LICENCED IP

- UIC – Exclusive license on LPC related IP

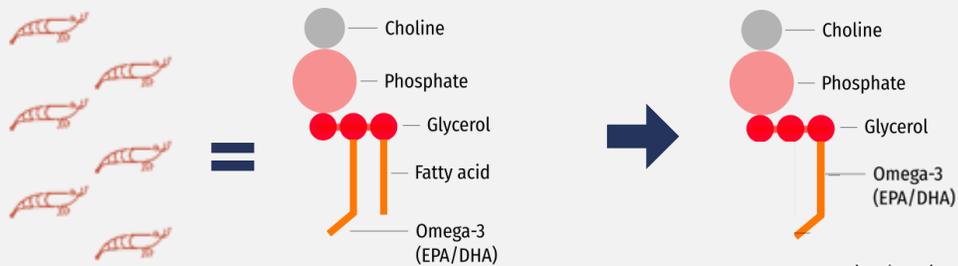
# Fully integrated value chain from Antarctica to Final product ensuring a cost-efficient production process

## FULLY INTEGRATED VALUE CHAIN



## UNIQUELY SUITED RAW MATERIAL

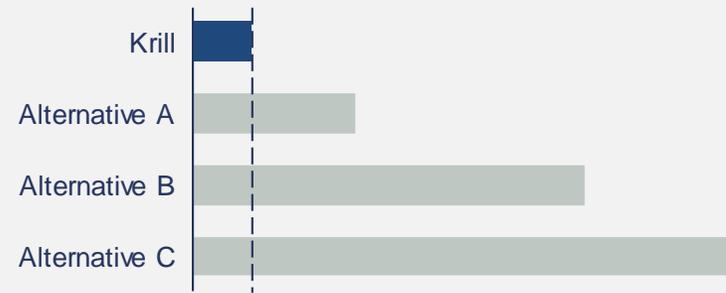
The krill phospholipid molecule has a close similarity to the LPC molecule



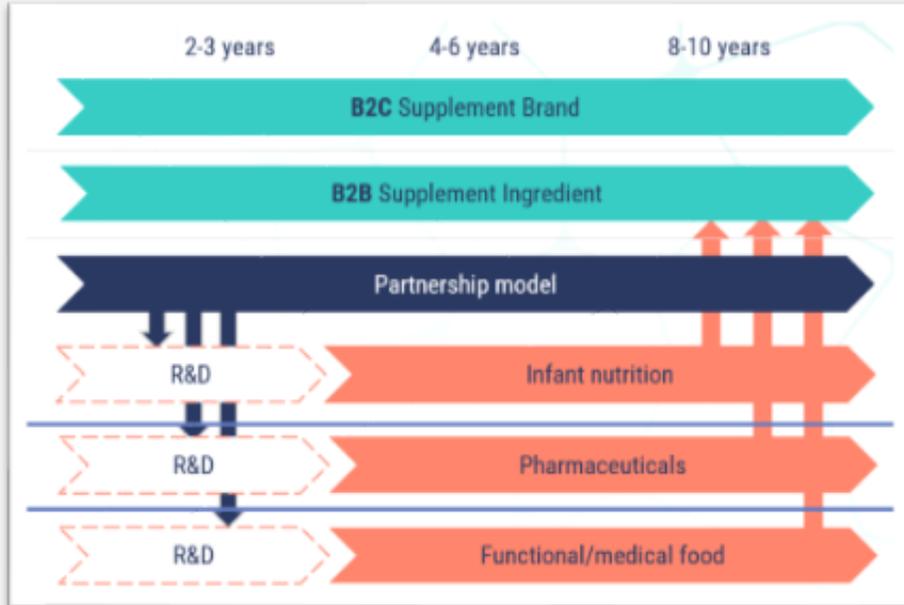
## COST EFFICIENT PRODUCTION PROCESS

Our IP-protected production process gives a much lower cost compared to all other known production processes

UNIT COST BY PRODUCTION ALTERNATIVES



# Developing the applications for LysovetA



Build the space across different segments through collaboration and partnerships

## COMMERCIAL PARTNERSHIPS

Partnership with Michael Davidson, targeting several indications across the space of Brain and Eye health

## SUPPLEMENT PRODUCT

Commercialize LPC-DHA/EPA dietary supplement product by the end of 2022

## RESEARCH & DEVELOPMENT

Collaboration and licence agreement with University Illinois Chicago

# Key deal highlights

## Indications covered by agreement



### EYE HEALTH

- Dry Age-Related Macular Degeneration
- Dry eye syndrome
- Stargardt's juvenile blindness



### BRAIN HEALTH

- ApoE4 related Alzheimer's
- Gestational diabetes and Zika infection related microcephaly

## Set up

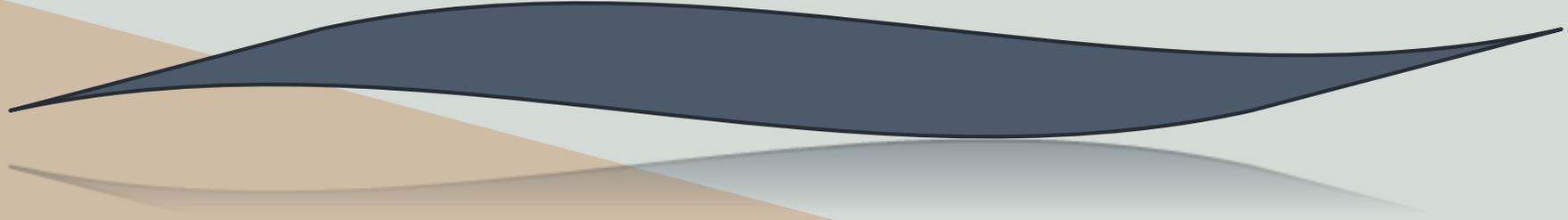
- Formation of a single purpose vehicle for the development of the therapies
- Raise approx. 30M USD to fund proof of concept clinical trials

## Aker BioMarines contributions

- Exclusive license under Aker BioMarine's IP, limited to the fields of the distinct therapies
- Supply of LPC API (LYSOVETA)

## Aker BioMarine's economics

- 50% equity prior to initial fundraising
- Milestones to fund Aker BioMarine's API manufacturing capabilities
- Double-digit royalties from commercial sales
- Payment of product supply



# **MD3 Solutions Investor Presentation**

*Novel Long-Chain Phospholipid Fatty Acids for Retinal and  
Brain Disorders*

*January 2021*

# MD3 Founder and Scientific Advisory Board

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## Management team



**Michael Davidson, MD, FACC, FNLA**

### Industry

- Founding CEO, CMO of Corvidia
  - Acquired by Novo Nordisk for \$2.1B
- Founder and CMO of Omthera
  - Acquired by AZ for \$443M in 2013
- CEO of New Amsterdam Pharma

### Academia

- Professor and Director of Preventive Cardiology at University of Chicago
- Coordinated >1,000 clinical trials in preventive cardiology
- Published >350 articles for leading medical journals
- Published three books on lipidology

## Scientific advisory board



**Alan Remaley, MD PhD**

- Section Chief of Lipoprotein Metabolism, NHLBI
- Inventor of process to synthesize Very-long chain PUFAs



**Papasani Subbaiah, PhD**

- Professor of Medicine and Biochemistry, University of Illinois
- World expert on omega-3's and inventor of phospholipid-omega-3's structure for brain and retina uptake

Partnered with Aker BioMarine

# Executive Summary

MD3 has partnered with Aker BioMarine to run a clinical program targeting retinal and brain disorders associated with low levels of long-chain omega-3 fatty acids

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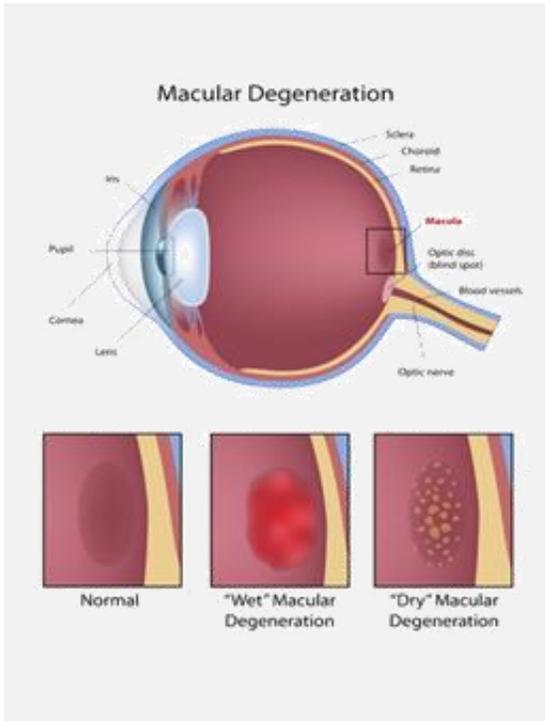
- The Company is founded around four new scientific discoveries – protected by IP – enabled by Aker BioMarine’s lysophosphatidylcholine (LPC) delivery mechanism<sup>1</sup>
  - The omega-3 transports (Mfsd2a) across the blood-brain barrier and LPC-DHA is the preferred substrate
  - LPC-DHA is absorbed directly into the plasma and protected from digestion into free DHA
  - Elongase enzymes 2 and 4 are required to synthesize DHA and other very-long chain polyunsaturated fatty acids (VLC-PUFAs) in the retina and diminish with age resulting in lower tissue omega-3 levels
  - VLC-PUFAs are required for normal photoreceptor function and genetic deficiency (ELVOLV 4)
  
- MD3 is planning on launching four proof of concept clinical programs based on these discoveries:
  - Complex mixture of LPC EPA and DHA for 1) dry eye , 2) age-related macular degeneration (AMD) and 3) ApoE4 associated Alzheimer’s Disease
  - Lower concentration LPC EPA / DHA based medical foods for 4) gestational diabetes or Zika infections to prevent Congenital Microcephaly
  
- Targeting a \$30 MUSD Series A round towards select investors to set up IND and run Proof-of-Concept human trials

<sup>1</sup>Transporter has shown in preclinical studies to be 6.75x more efficient crossing the blood-brain/eye barrier than traditional molecule forms of EPA/DHA

# Initial Target Opportunities

Potential to address significant unmet medical needs across a variety of indications

**Dry AMD more than 10M in USA-no approved therapies > \$20B potential**



**Dry Eye**-The liquid drops are the largest segment of the dry eye medication market, accounting for \$4B in 2019 sales- efficacy of present therapies is limited



**35% of patients with Alzheimer's have apoE4-impaired blood barrier protection and DHA metabolism**



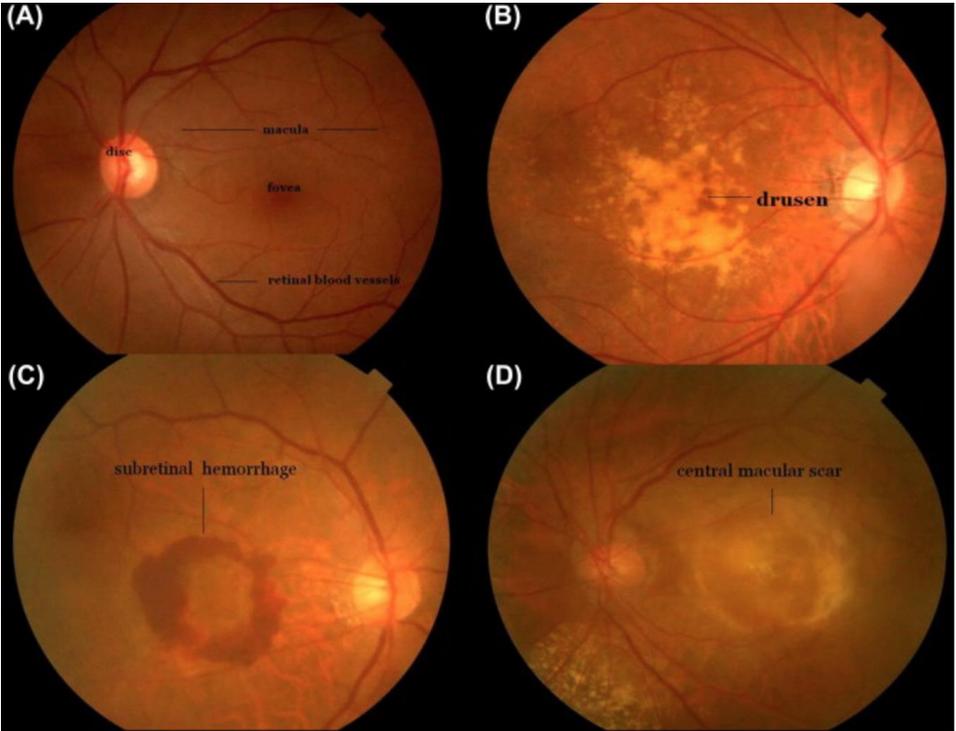
**Gestational Diabetes**- Every year, 2% to 10% of pregnancies in the United States are affected by gestational diabetes- resulting in lower DHA uptake in the fetus associated with congenital brain abnormalities



# Ophthalmic Indications for LPC OM3 include AMD (geographic atrophy) and dry eye

Docosahexaenoic acid (DHA) is a major lipid component of retinal photoreceptor outer segment membranes that has anti-inflammation and anti-angiogenesis properties that could protect against AMD. Low DHA levels correlate with progression of AMD

Topical administration with DHA accelerates the regeneration of corneal nerves after their damage during corneal surgery, promoting the return of sensitivity and reducing the signs of dry eye.



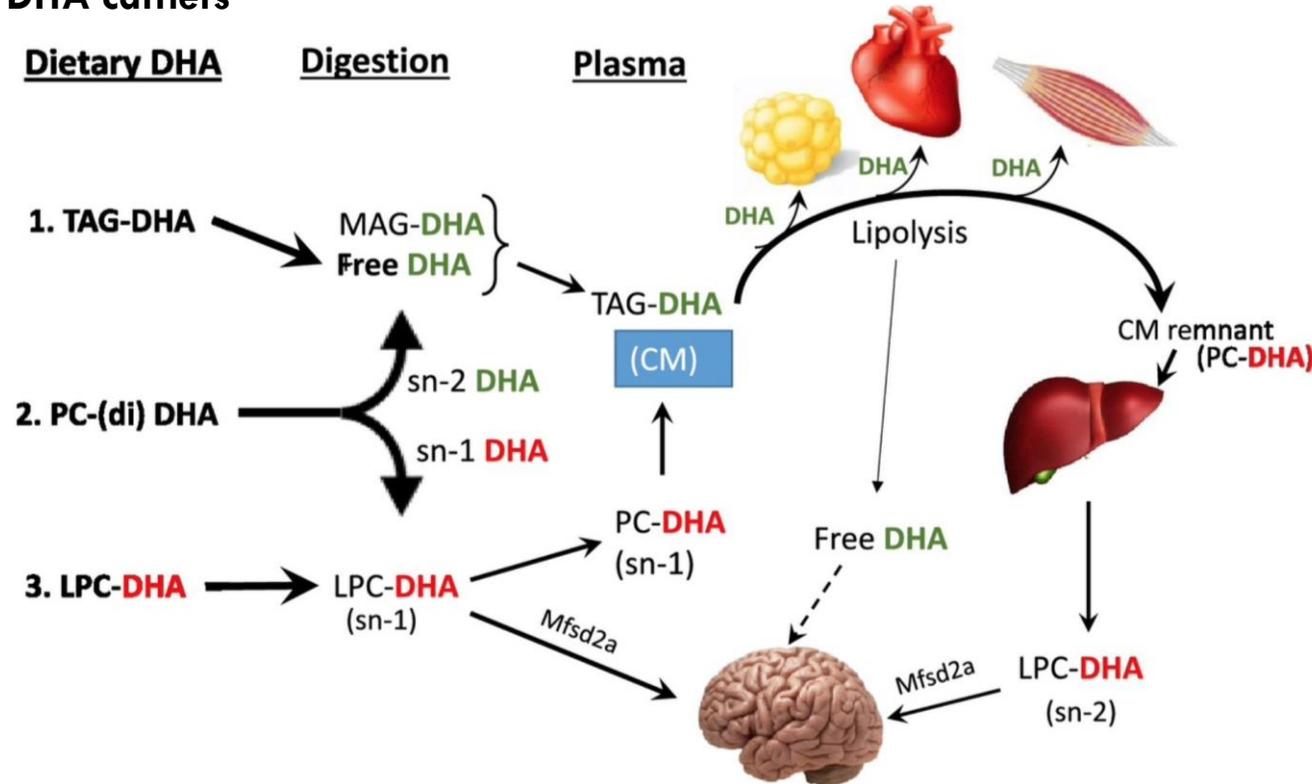
# Unique Delivery Mechanism Opens the Playing Field

Novel discovery: the *Mfsd2a* transporter across the blood-brain barrier prefers LPC omega-3

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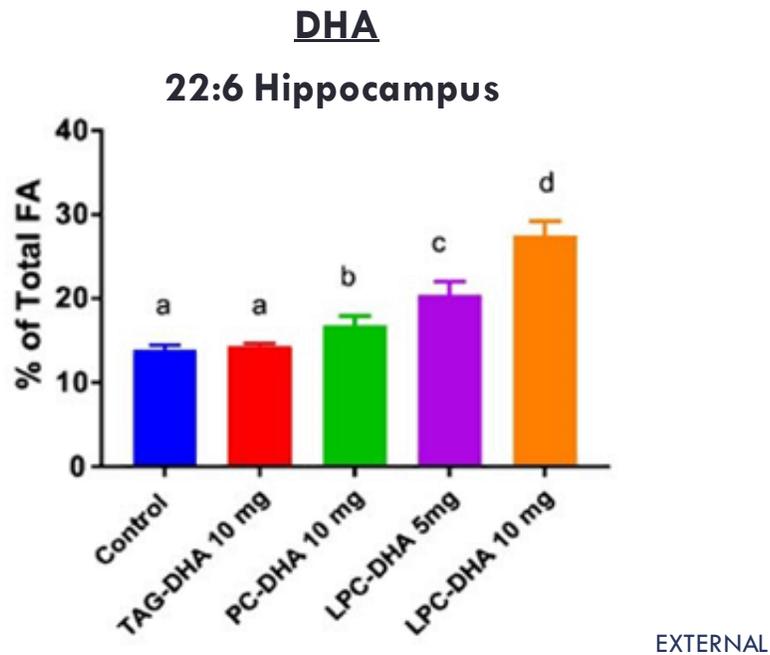
LPC-DHA (and EPA) are preferentially transported by *Mfsd2a* compared to other omega-3's

## Metabolic fates of dietary DHA carriers

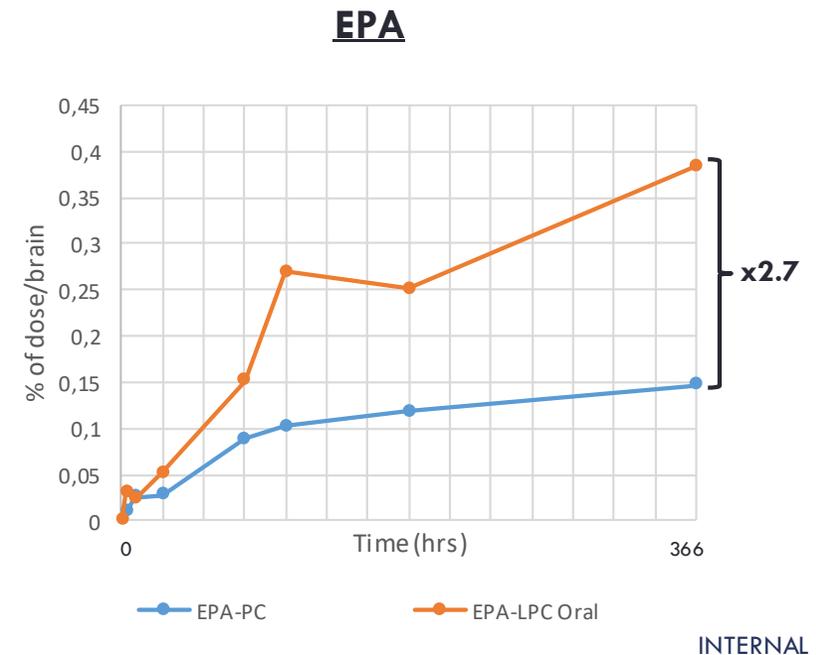


# Brain Uptake: ~2 Times Higher Increase of EPA/DHA in the Brain When It Is Administered As LPC Compared to PC

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DHA uptake from LPC significantly higher than from PC, which is again significantly higher than TG



EPA uptake from oral admin of LPC-EPA ~2.7X higher than from oral admin of PC-EPA

# Opportunities Across a Breadth of Indications (cont'd)

## ApoE4 genotype associated with impaired DHA transport across the blood-brain barrier

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### ApoE4 genotype associated with impaired DHA metabolism and brain uptake

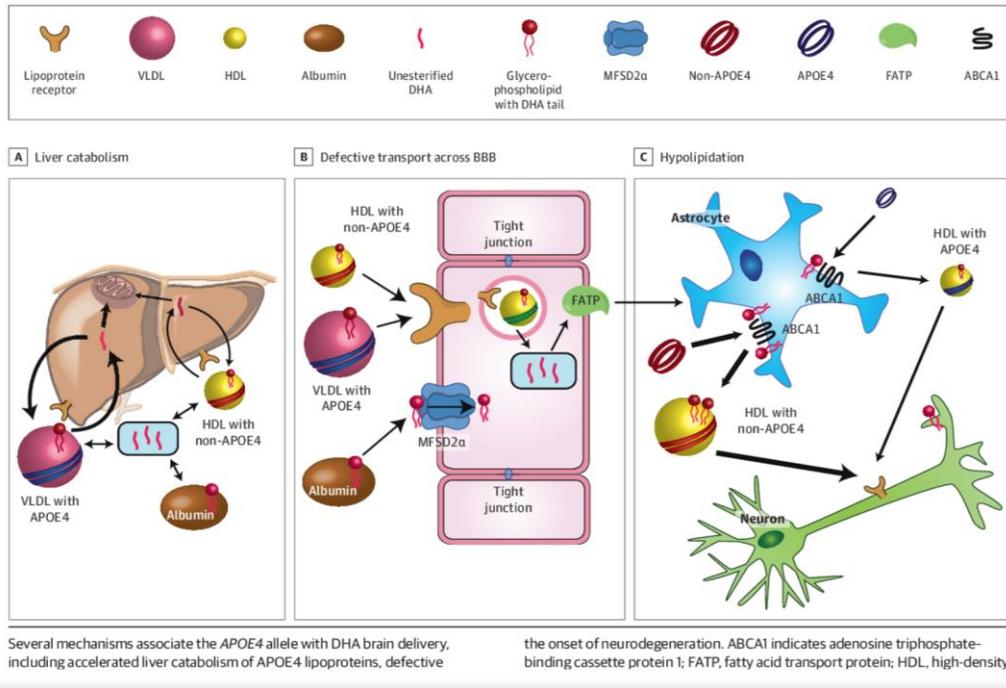
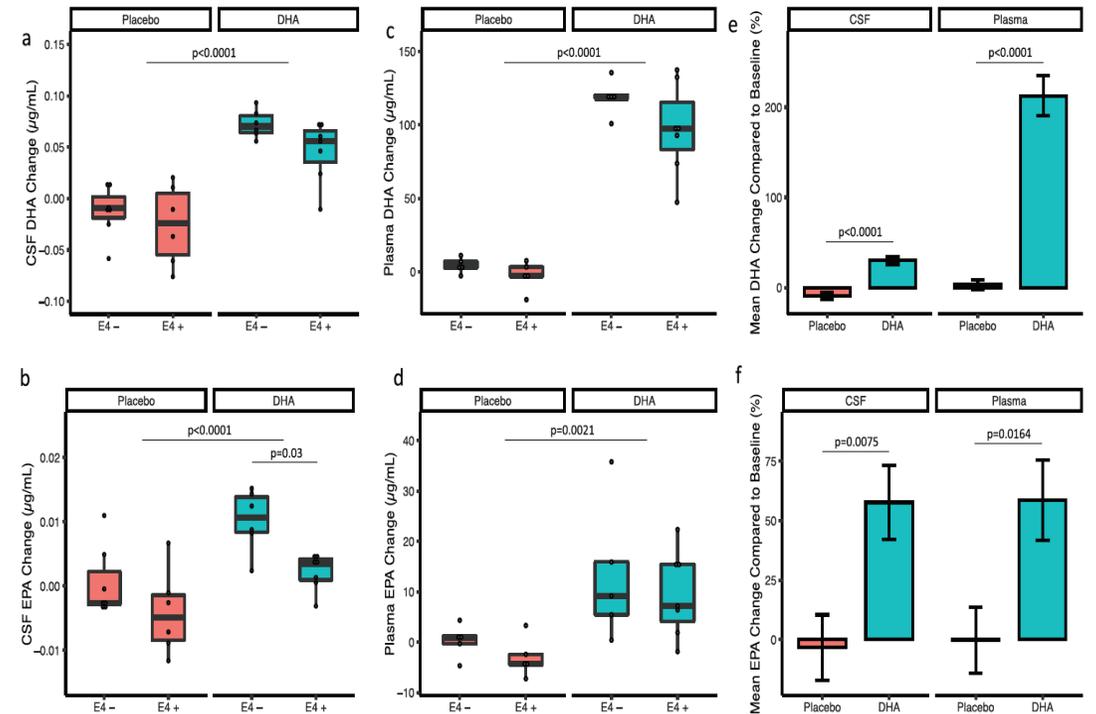


Figure 1. Mechanisms Linking Apolipoprotein E 4 (APOE4) Status With Docosahexaenoic Acid (DHA) Delivery to the Brain Before the Onset of Neurodegeneration

### ApoE4 have lower CSF levels of DHA and significantly decreased uptake after high dose supplementation



# Cost and timeline - 30 MUSD to reach POC for targeted indications

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Cost	Area	Activity	2021				2022				2023			
			Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
6MUSD	Process and preparations	Product adjustments LPC-EPA/DHA	█											
		IND Enabling studies			█									
9MUSD	Dry AMD	Phase 1 / 2a - POC geographic atrophy progression					█							
6MUSD	Dry eye syndrome	POC clinical study					█							
3MUSD	ApoE4 Alzheimers	POC by measurement of CSF levels of DHA					█							
2MUSD	Geststional diabetes	POC Maternal measurement of DHA levels					█							
2MUSD	SG&A	2MUSD/year	█											

# Investment Highlights

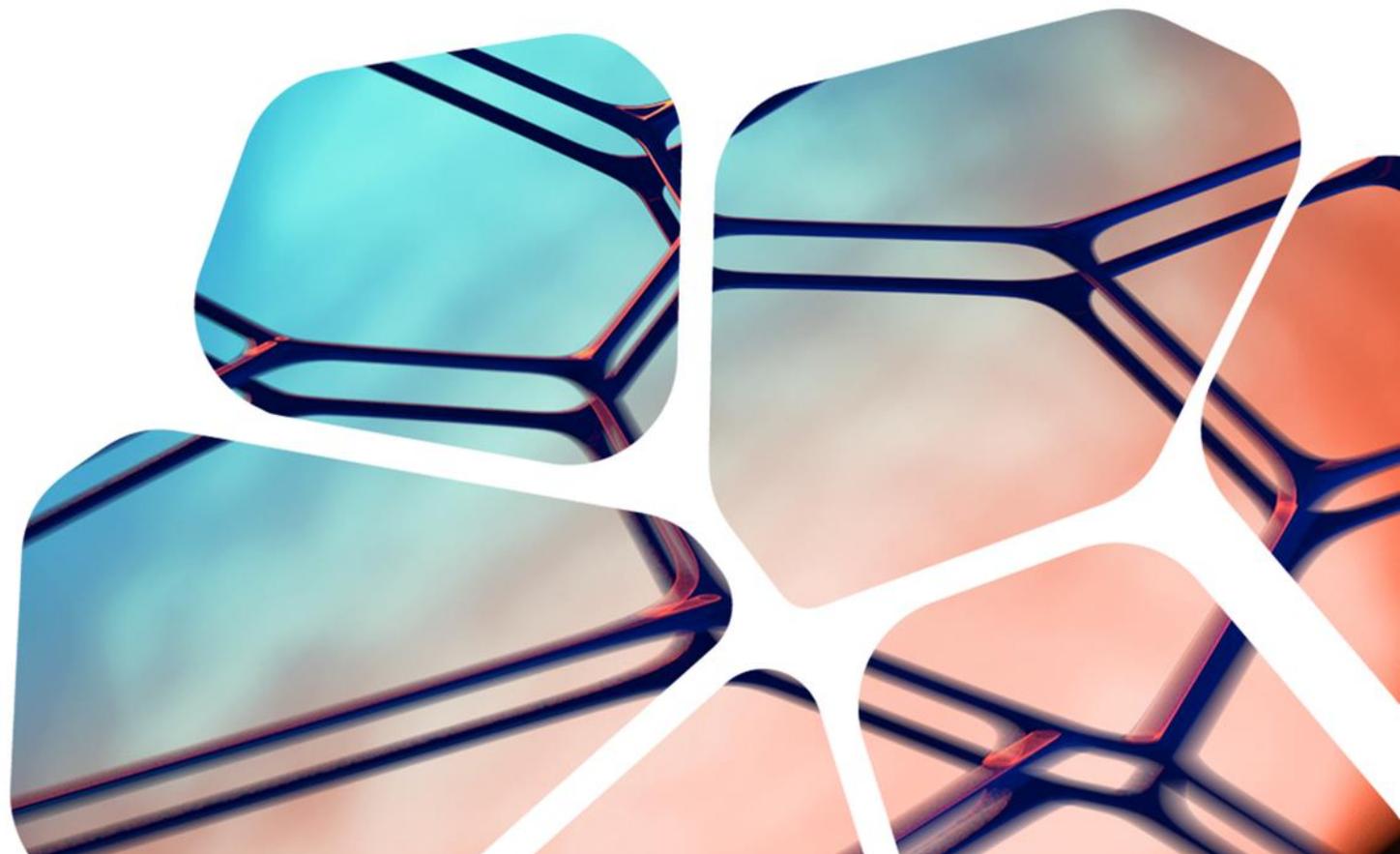
MD3 has partnered with Aker BioMarine to Develop LPC-PUFAs for Eye and Brain Disorders

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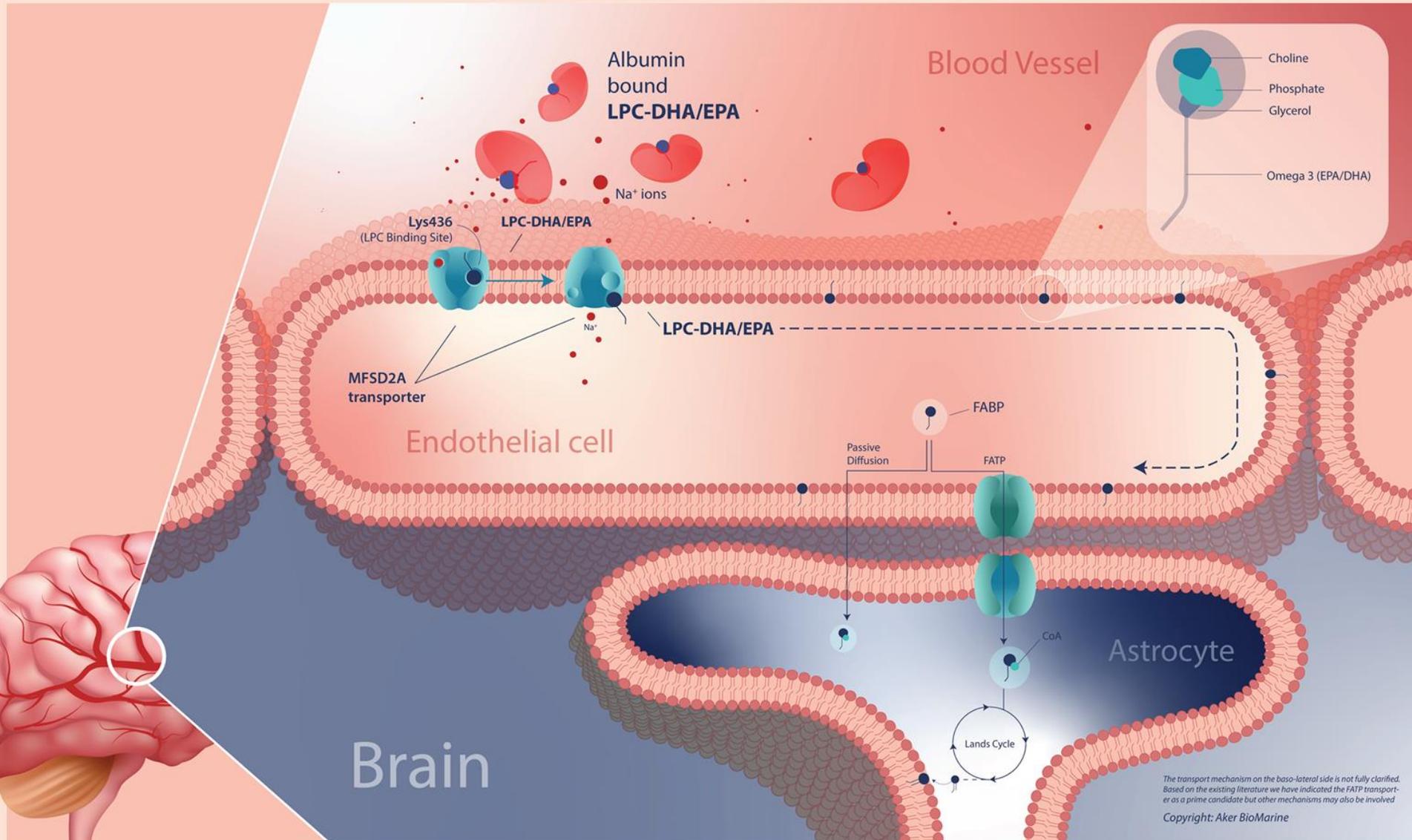
**\$30M provides clinical proof of concept within two years for 4 major indications with blockbuster potential**

- ❑ Dry age associated macular degeneration (geographic atrophy)-the leading cause of blindness
- ❑ Eye drops solution for dry eye- the most common condition requiring a visit to an Ophthalmologist
- ❑ ApoE4 associated Alzheimer's Disease- 60% of patients with dementia linked to low CSF DHA levels
- ❑ Gestational Diabetes and Zika infections- associated with congenital brain disorders linked to low DHA levels
- ❑ Orphan path for Stargardts Type 3 with LPC-VLC-PUFA- combining Aker BioMarine and NIH IP for optimal eye delivery
- ❑ Experienced Team for Clinical Development and Manufacturing of Novel Pharmaceutical products

# APPENDIX



# LPC-DHA/EPA transport through the Blood-Brain Barrier



1. Lagarde, M., et al., Lysophosphatidylcholine as a preferred carrier form of docosahexaenoic acid to the brain. *Journal of Molecular Neuroscience*, 2001. 16(2-3): p. 201-4.

2. Nguyen, L.N., et al., Mfsd2a is a transporter for the essential omega-3 fatty acid docosahexaenoic acid. *Nature*, 2014. 509(7501): p. 503-6.

3. Quek, D.Q., et al., Structural Insights into the Transport Mechanism of the Human Sodium-dependent Lysophosphatidylcholine Transporter MFS2A. *J Biol Chem*, 2016. 291(18): p. 9383-94.

4. Yalagala, P.C.R., et al., Lipase Treatment of Dietary Krill Oil, but Not Fish Oil, Enables Enrichment of Brain Eicosapentaenoic Acid and Docosahexaenoic Acid. *Mol Nutr Food Res*, 2020. 64(12): p. e2000059.

5. Sugasini, D., P.C.R. Yalagala, and P.V. Subbaiah, Efficient Enrichment of Retinal DHA with Dietary Lysophosphatidylcholine-DHA: Potential Application for Retinopathies. *Nutrients*, 2020. 12(10).

6. Wong, B.H. and D.L. Silver, Mfsd2a: A Physiologically Important Lysolipid Transporter in the Brain and Eye. *Adv Exp Med Biol*, 2020. 1276: p. 223-234.

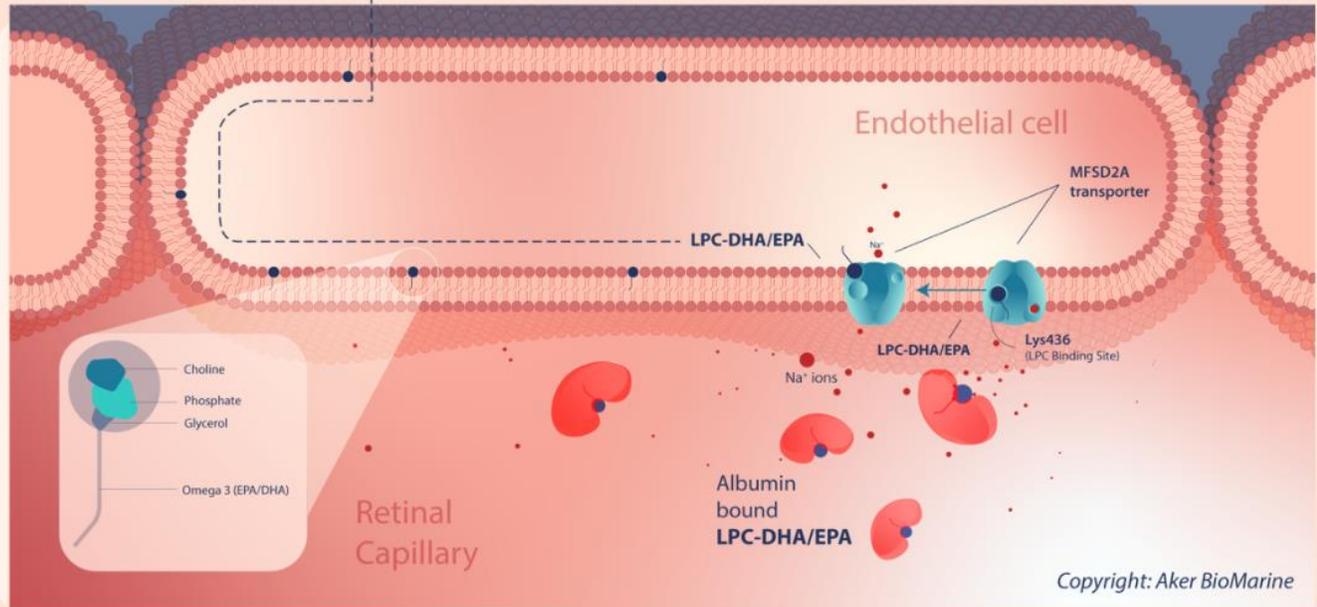
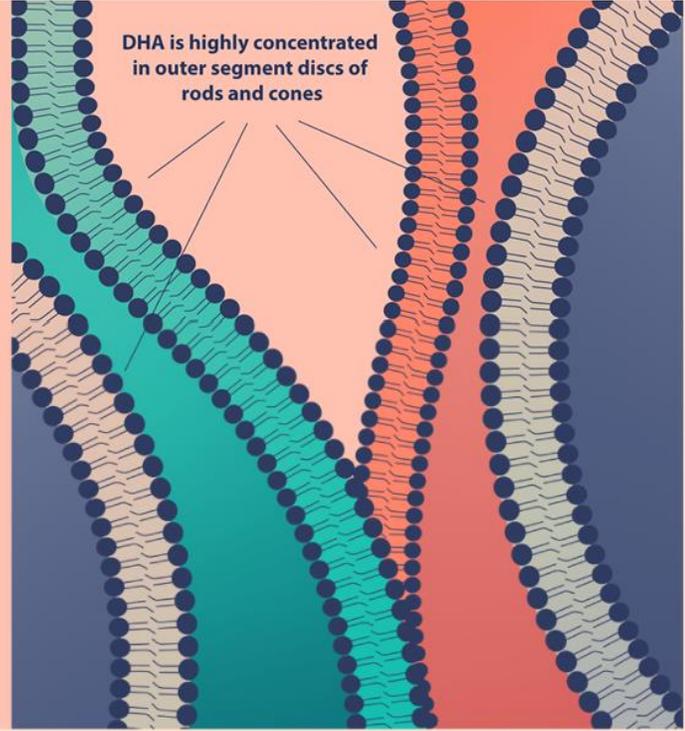
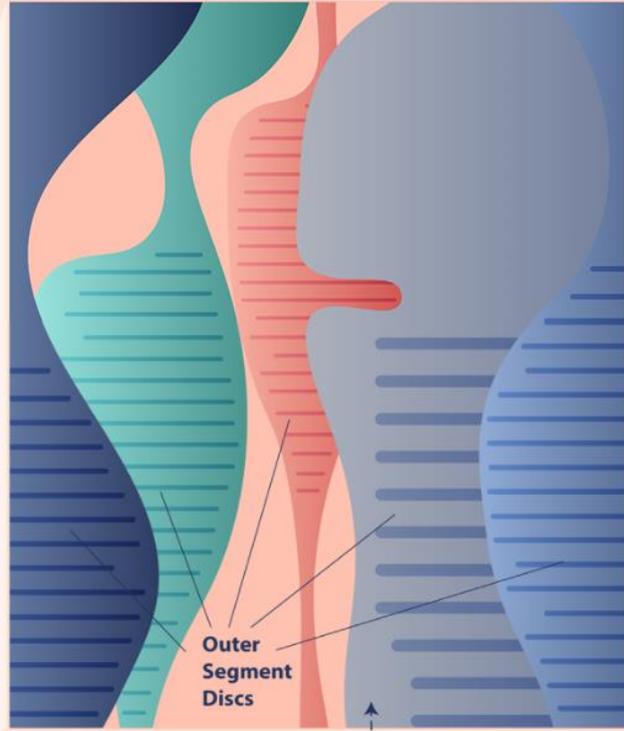
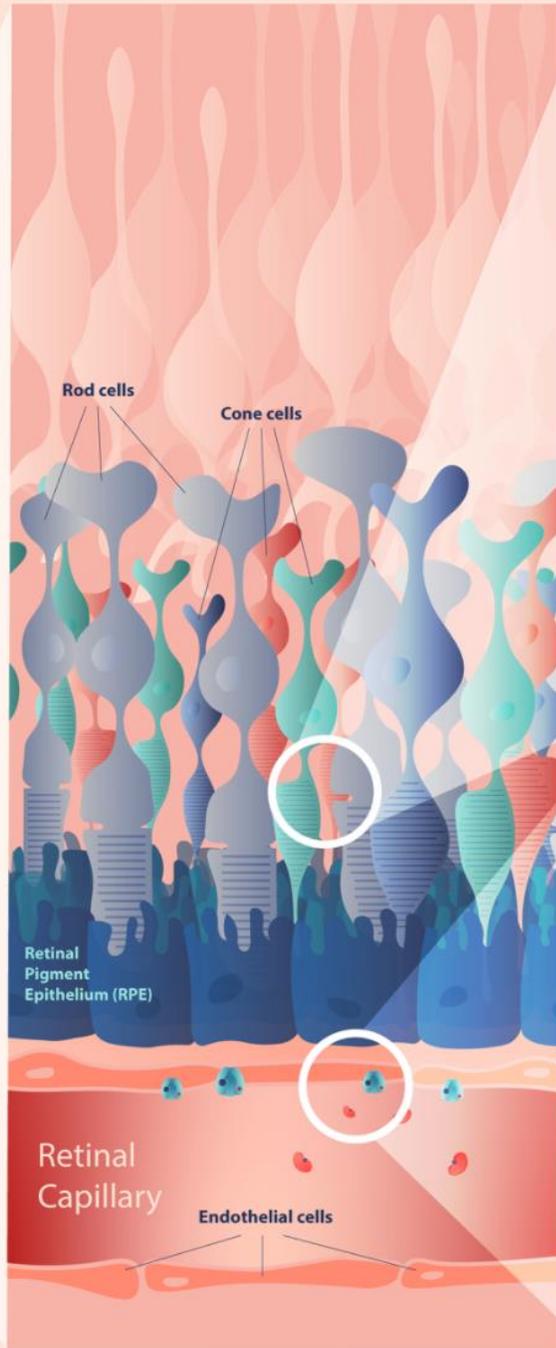
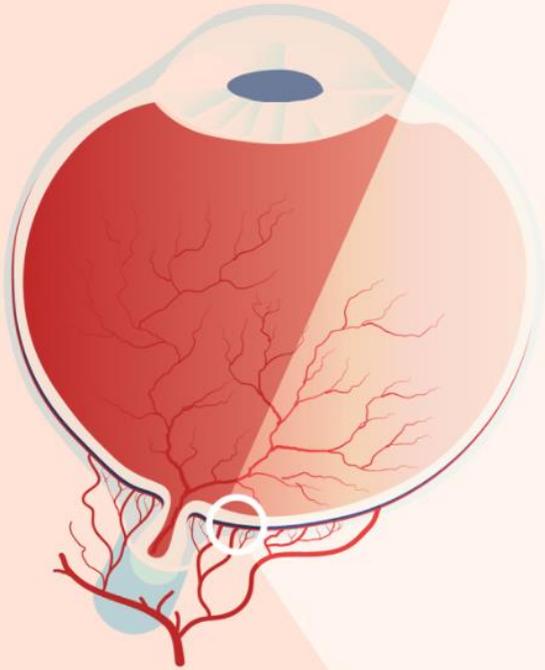
7. Wong, B.H., et al., Mfsd2a Is a Transporter for the Essential  $\omega$ -3 Fatty Acid Docosahexaenoic Acid (DHA) In Eye and Is Important for Photoreceptor Cell Development. *J Biol Chem*, 2016. 291(20): p. 10501-14.

8. Sugasini, D., et al., Dietary docosahexaenoic acid (DHA) as lysophosphatidylcholine, but not as free acid, enriches brain DHA and improves memory in adult mice. *Sci Rep*, 2017. 7(1): p. 11263.

9. Alakbarzade, V., et al., A partially inactivating mutation in the sodium-dependent lysophosphatidylcholine transporter MFS2A causes a non-lethal microcephaly syndrome. *Nat Genet*, 2015. 47(7): p. 814-7.

10. Bazinet, R.P. and S. Laye, Polyunsaturated fatty acids and their metabolites in brain function and disease. *Nature Reviews Neuroscience*, 2014. 15(12): p. 771-85.

# LPC-DHA/EPA transport into the Eye



1. Wong, B.H., et al., *Mfsd2a is a Transporter for the Essential ω-3 Fatty Acid Docosahexaenoic Acid (DHA) in Eye and Is Important for Photoreceptor Cell Development.* *J Biol Chem*, 2016. 291(20): p. 10501-14.

2. Lobanova, E.S., et al., *Disrupted Blood-Retina Lysophosphatidylcholine Transport Impairs Photoreceptor Health But Not Visual Signal Transduction.* *The Journal of Neuroscience*, 2019. 39(49): p. 9689-9701.

3. Wong, B.H. and D.L. Silver, *Mfsd2a: A Physiologically Important Lysolipid Transporter in the Brain and Eye.* *Adv Exp Med Biol*, 2020. 1276: p. 223-234. 2.

4. Sugasini, D., P.C.R. Yalagala, and P.V. Subbaiah, *Efficient Enrichment of Retinal DHA with Dietary Lysophosphatidylcholine-DHA: Potential Application for Retinopathies.* *Nutrients*, 2020. 12(10).

# Aker BioMarine LPC-portfolio and in-license

AKBM IP	Status	Claims
<p><b>Phospholipid capsules</b></p> <p><b>US10117882 (B2),</b></p>	<p><b>Filed Aug 4, 2010</b></p> <p><b>Granted</b> <b>(Nov 6, 2018)</b></p>	<p><b>Gel capsules:</b></p> <ul style="list-style-type: none"> <li>- Mix of PL</li> <li>- At least 15-45 % w/w of all types of lyso-PL (LPC, LPE, LPS, LPI) in mix with other PL.</li> <li>- Independent of origin</li> <li>- At least 1 % EPA or DHA</li> </ul>
<p><b>LPC-EPA</b></p> <p><b>US 10555957 (B2)</b></p>	<p><b>Filed May 10, 2018</b></p> <p><b>Granted – Exclusive license</b> <b>(Feb 11, 2020)</b></p>	<p><b>LPC-EPA:</b></p> <ul style="list-style-type: none"> <li>- Formulations comprising the compound</li> <li>- Medical method</li> </ul>
<p><b>Phospholipid capsules</b></p> <p><b>US10525068 (B2)</b></p>	<p><b>Filed March 7, 2019</b></p> <p><b>Granted</b> <b>(Jan 7, 2020)</b></p>	<p><b>Gel capsules:</b></p> <ul style="list-style-type: none"> <li>- Mix of PL, independent of origin</li> <li>- At least 15-60 % w/w of all types of lyso-PL (LPC, LPE, LPS, LPI).</li> <li>- At least 1 % EPA or DHA</li> <li>- TG</li> </ul>
<p>LPC-compositions</p> <p>WO2019123015 (A1)</p> <p>KR, AU, NZ, ID, EUR, IN, EP, BR, US, CA, SG, CN, JP, MX, IL</p>	<p>Filed Des 21, 2018</p> <p>Pending (National phases – 15 countries)</p>	<p><b>LPC Composition</b></p> <ul style="list-style-type: none"> <li>- Natural sources, marine origin</li> <li>- 10-100% w/w LPC</li> <li>- 5-50 % w/w omega-3</li> </ul>
<p>Phospholipid compositions</p> <p>US Appl No No. 16/734,850</p>	<p>Filed Jan 6, 2020</p> <p>Pending</p>	<p><b>Lipid composition:</b></p> <ul style="list-style-type: none"> <li>- Mix of PL</li> <li>- At least 15-60 % w/w of all types of lyso-PL (LPC, LPE, LPS, LPI)</li> <li>- At least 1 % EPA or DHA</li> <li>- TG</li> </ul>
<p>Pharmaceutical LPC-composition</p> <p>WO2020254675 (A1)</p>	<p>Filed June 21, 2020</p> <p>PCT-application (International phase)</p>	<p><b>Pharmaceutical LPC-composition</b></p> <ul style="list-style-type: none"> <li>- Medical use/methods</li> </ul>

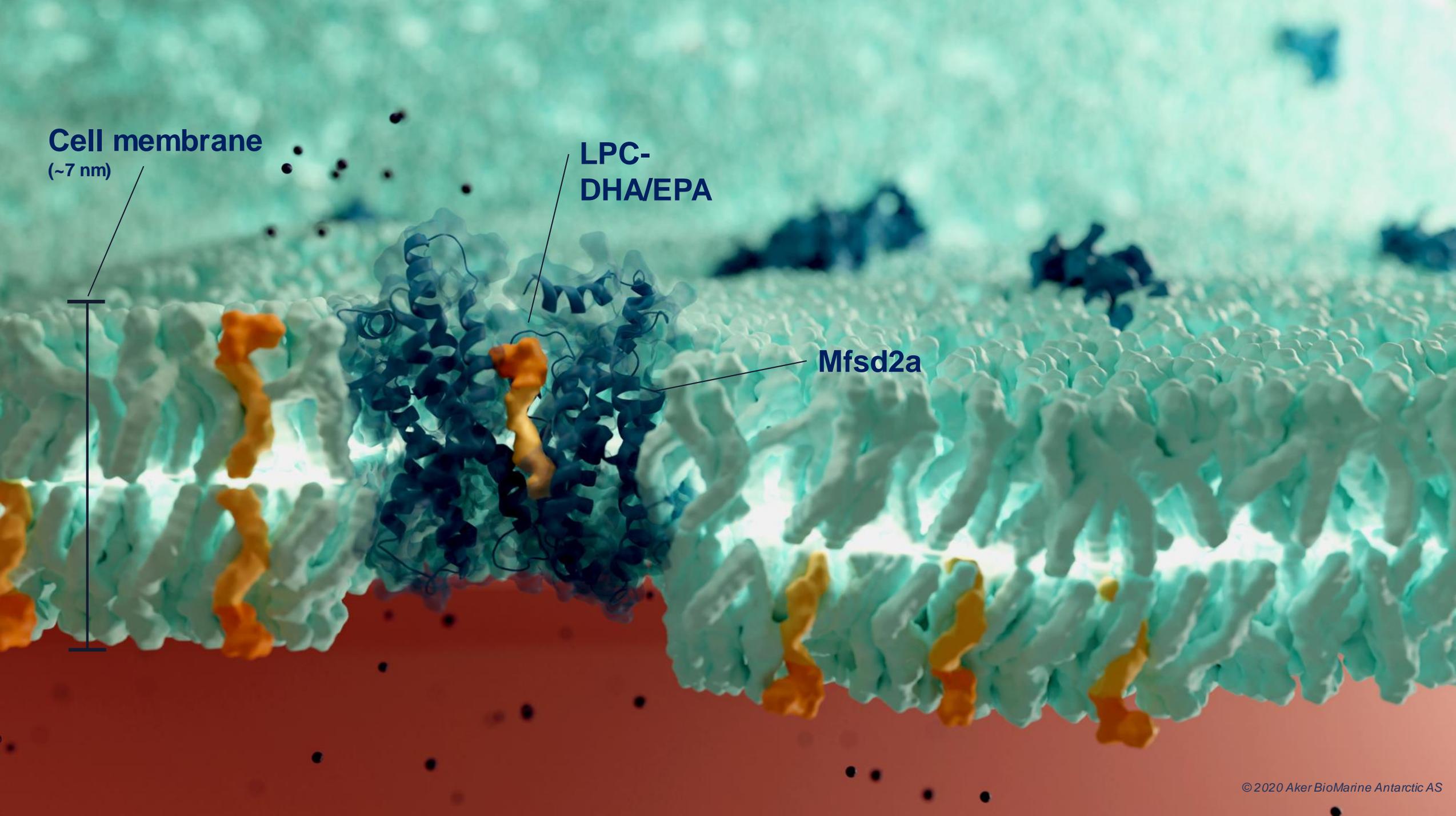
# Aker BioMarine IP overview – Krill oil portfolio

Product	Patents/applications	Claims
Krill oil (NKO)	1 patent family – 7 granted patents 1999/2002 priority Geographical scope: USA, Canada and Australia	<ul style="list-style-type: none"> <li>• Krill oil with &gt;40%PL and &gt;15 % omega-3</li> <li>• Contains EPA-PL or DHA-PL</li> </ul>
Krill oil (Superba)	1 patent family - 25 granted/validated patents, 1 pending application 2007 priority Geographical scope: USA, EU, Canada and Australia	<ul style="list-style-type: none"> <li>• Krill oil w/ defined PLs</li> <li>• Extraction from krill meal, not limited to any specified extraction method</li> </ul>
Krill oil (Enzymotec)	2 patent families- 21 granted/validated patents, 6 pending applications Priorities from 2014 Geographical scope: EU, USA, Australia, ZA, MY, CN	<ul style="list-style-type: none"> <li>• Krill oil with low TMAO</li> <li>• Krill oil w/ specified ratio between different fatty acids</li> </ul>
Purified krill oil	3 patent families – 9 granted – 11 pending applications Priority from 2013 and 2015 Geo scope: US, EU, AUS, CN, BR, ID, KR, NZ, RU,	<ul style="list-style-type: none"> <li>• Extraction and purification processes, washing cycles</li> <li>• Clean 2<sup>nd</sup> generation krill oil with e.g. low salt, TMAO, arsenic and copper levels, FlexiTech process</li> </ul>
Uses	2 patent families Priority from 2007-14	<ul style="list-style-type: none"> <li>• Metabolic syndrome and appetite reduction</li> <li>• Brain age – ADHD</li> </ul>
Others	6 patent families related to different krill oil formulations Priorities from 2012-2014. Mostly US, some also in EP, CA, AU	<ul style="list-style-type: none"> <li>• High PL-content formulations</li> <li>• Krill oil compositions, capsules, pre-formulations with PL-content above 85%.</li> <li>• Krill oil + TG/EE (fish oil)</li> <li>• Krill oil with improved viscosity</li> </ul>

**Cell membrane**  
(~7 nm)

**LPC-  
DHA/EPA**

**Mfsd2a**





# LYSOVETA

LPC-DHA/EPA

