



AKER BIOMARINE



LYSOVETA™

Launching molecule delivery platform with broad application potential

By

CEO, Matts Johansen

Director R&D, Andreas Storsve, PhD Cognitive Neuroscience

IN 2014 BREAK-THROUGH SCIENCE WAS PUBLISHED IDENTIFYING MFSD2A AS A KEY TRANSPORTER OF DHA/EPA ACROSS THE BLOOD BRAIN BARRIER



14th of May 2014

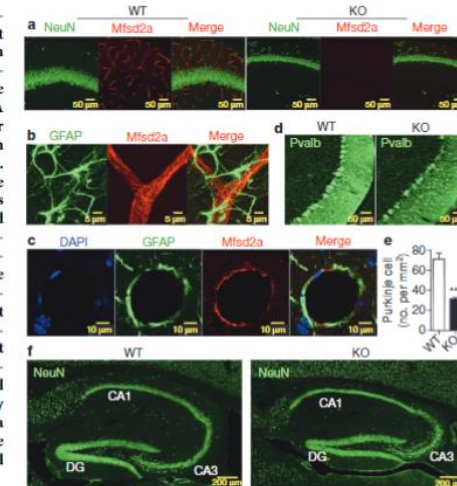
LETTER

doi:10.1038/nature13241

Mfsd2a is a transporter for the essential omega-3 fatty acid docosahexaenoic acid

Long N. Nguyen¹, Dongliang Ma², Guanghou Shui³, Peiyan Wong², Amaury Cazenave-Gassiot³, Xiaodong Zhang², Markus R. Wenk³, Eyleen L. K. Goh² & David L. Silver¹

Docosahexaenoic acid (DHA) is an omega-3 fatty acid that is essential for normal brain growth and cognitive function^{1–4}. Consistent with its importance in the brain, DHA is highly enriched in brain phospholipids^{5–7}. Despite being an abundant fatty acid in brain phospholipids, DHA cannot be *de novo* synthesized in brain and must be imported across the blood–brain barrier, but mechanisms for DHA uptake in brain have remained enigmatic. Here we identify a member of the major facilitator superfamily—Mfsd2a (previously an orphan transporter)—as the major transporter for DHA uptake into brain. Mfsd2a is found to be expressed exclusively in endothelium of the blood–brain barrier of micro-vessels. Lipidomic analysis indicates that *Mfsd2a*-deficient (*Mfsd2a* knockout) mice show markedly reduced levels of DHA in brain accompanied by neuronal cell loss in hippocampus and cerebellum, as well as cognitive deficits and severe anxiety, and microcephaly. Unexpectedly, cell-based studies indicate that Mfsd2a transports DHA in the form of lysophosphatidylcholine (LPC), but not unesterified fatty acid, in a sodium-dependent manner. Notably, Mfsd2a transports common plasma LPCs carrying long-chain fatty acids such as LPC oleate and LPC palmitate, but not LPCs with less than a 14-carbon acyl chain. Moreover, we determine that the phosphor-zwitterionic headgroup of LPC is critical for transport. Importantly, *Mfsd2a*-knockout mice have markedly reduced uptake of labelled LPC DHA, and other LPCs, from plasma into brain, demonstrating that Mfsd2a is required for brain uptake of DHA. Our findings reveal an unexpected essential physiological role of plasma-derived LPCs in brain growth and function.



Since then this article has been cited >500 times, showing increasing interest in this emerging field of research

**SINCE THEN WE HAVE INVESTED IN RESEARCH, DEVELOPMENT, IP-RIGHTS AND
COMMERCIALIZATION STRATEGIES**

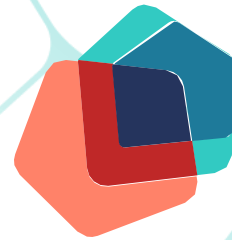
6 YEARS OF...

PRODUCT AND PROCESS DEVELOPMENT

RESEARCHING MECHANISMS AND EFFECTS

DEVELOPING IP-PROTECTION

BUILDING COMMERCIALIZATION STRATEGIES

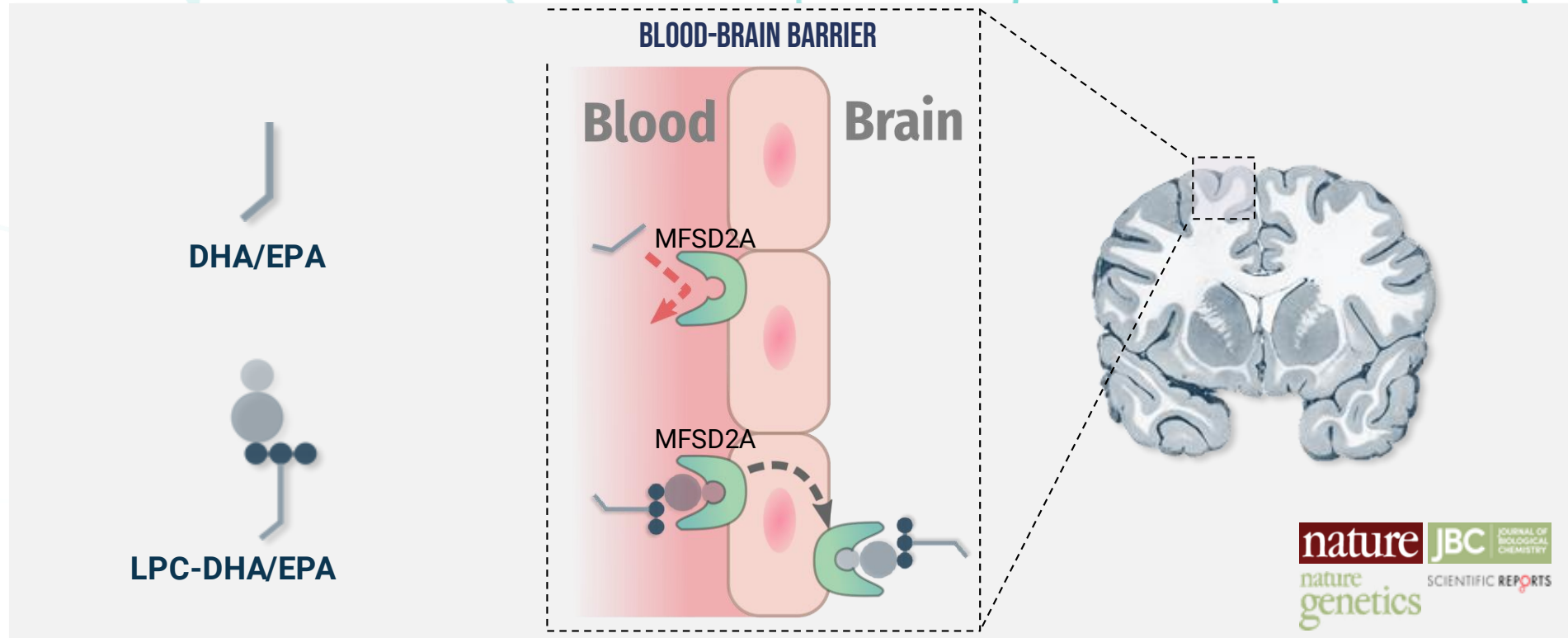


LYSOVETA™



AKER BIOMARINE

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

THE MFSD2A TRANSPORTER IS EXPRESSED IN A NUMBER OF VITAL ORGANS, INDICATING A BROAD APPLICATION POTENTIAL FOR LYSOVETA™

EYE

BREAST

KIDNEY

LIVER

PLACENTA

COLON

BRAIN

THYROID

LUNG

BONE MARROW

SKIN

LYMPH NODES

TESTES

INDEPENDENT PUBLISHED STUDIES DEMONSTRATE CLEAR BENEFITS OF LYSOVETA™ AS A DELIVERY PLATFORM FOR EPA AND DHA TO THE BRAIN AND EYE



X2

UPTAKE BRAIN

LPC-DHA showed twice the amount of DHA in the brain relative to free DHA

X7

MEMORY

LPC-DHA showed seven times better performance on a short-term memory test relative to free DHA

X2

PLASTICITY

LPC-DHA showed twice the amount of nerve growth factor BDNF in the brain relative to free DHA

X2

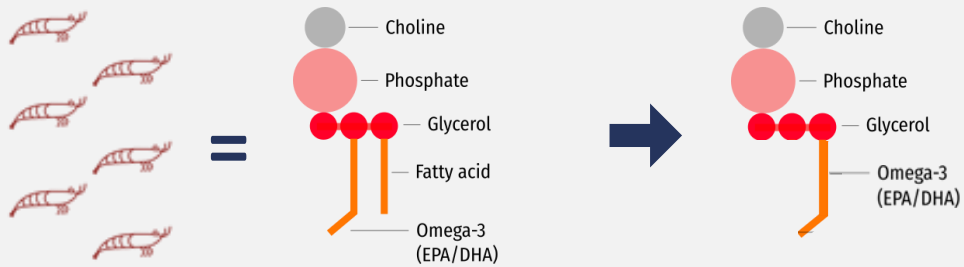
UPTAKE EYE

LPC-DHA is taken up twice as efficient in the retina relative to free DHA. LPC-EPA shows substantial increase in uptake relative to free EPA

UNIQUELY SUITED RAW MATERIAL, COST EFFICIENT PROCESS AND STRONG IP PROTECTION PROVIDES ATTRACTIVE COMPETITIVE POSITION

UNIQUELY SUITED RAW MATERIAL

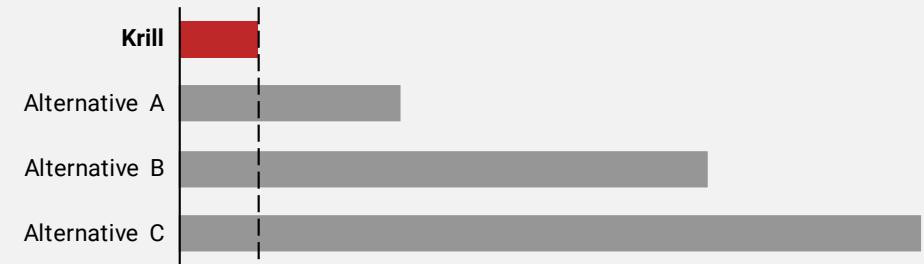
The krill phospholipid molecule has a close similarity to the LPC molecule



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



STRONG IP PROTECTION IN THE LPC SPACE

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

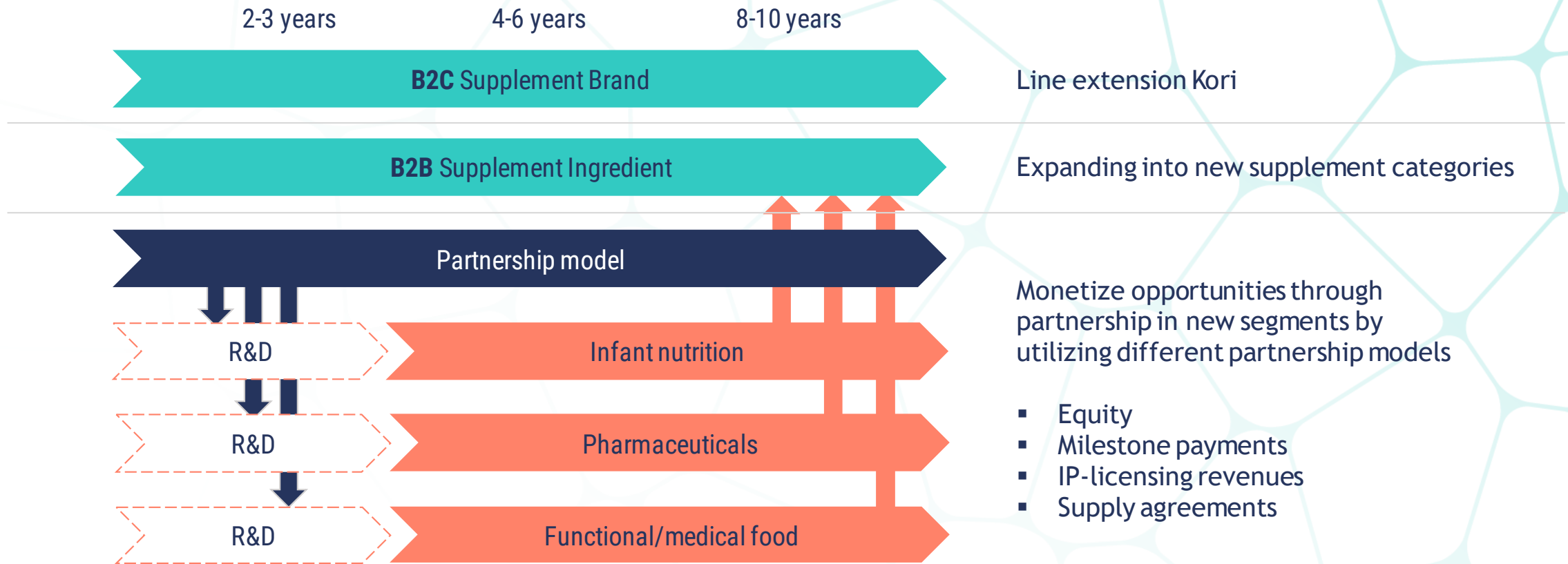
LPC SPECIFIC IP

- 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

WE HAVE THE AMBITION AND ABILITY TO THE LEAD DEVELOPMENT AND COMMERCIALIZATION OF ALL LYSOVETA™ RELATED OPPORTUNITIES



TAPPING INTO LARGE GLOBAL MARKETS WITH STRONG UNDERLYING DRIVERS



Brain health supplement sales shows ~20% YoY increase in the US



Depression alone accounts for 12% of healthy years lost

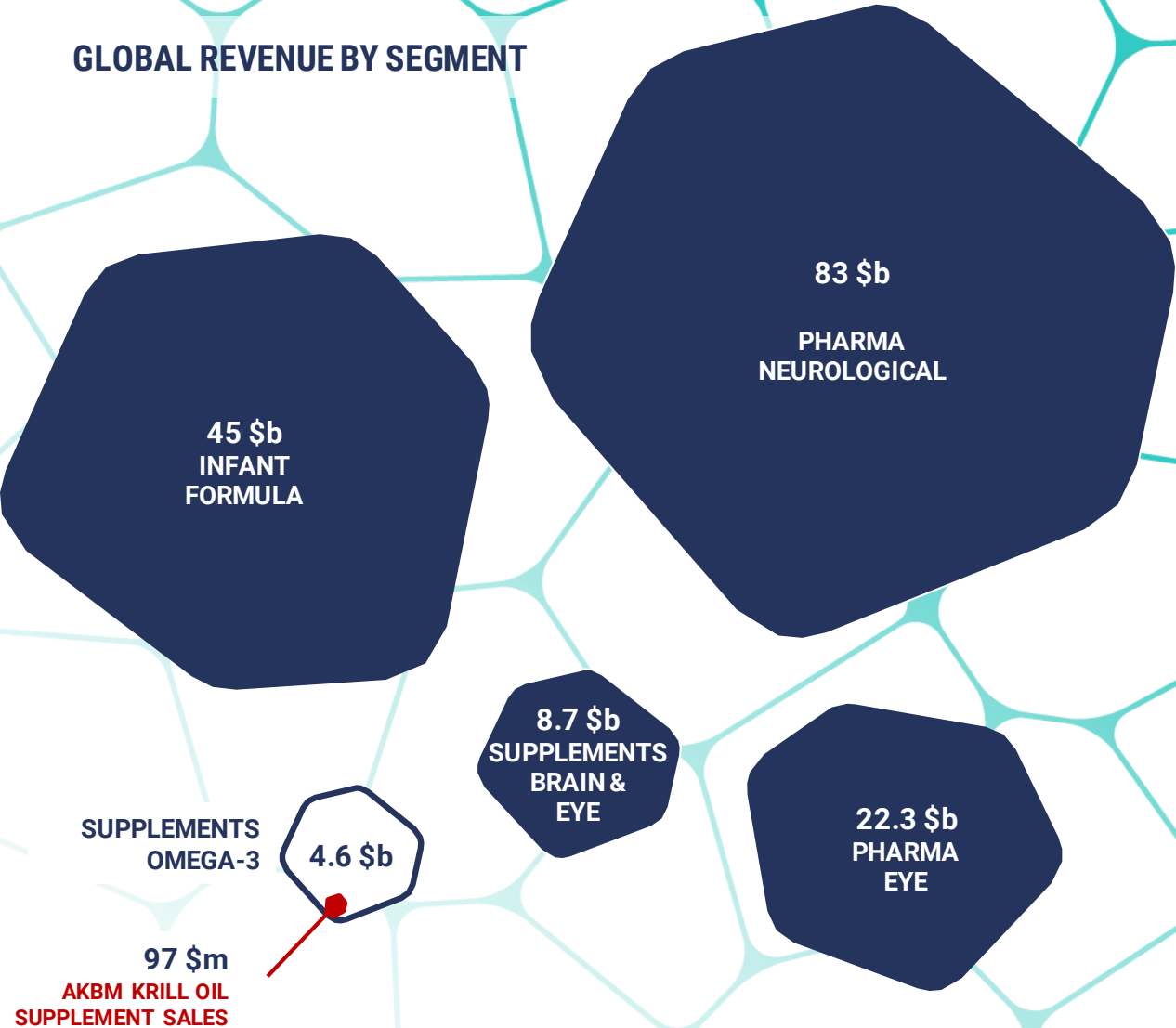


35% of adults > 60 in the US are concerned about losing memory



23% increase in ocular conditions in US over last 10 years

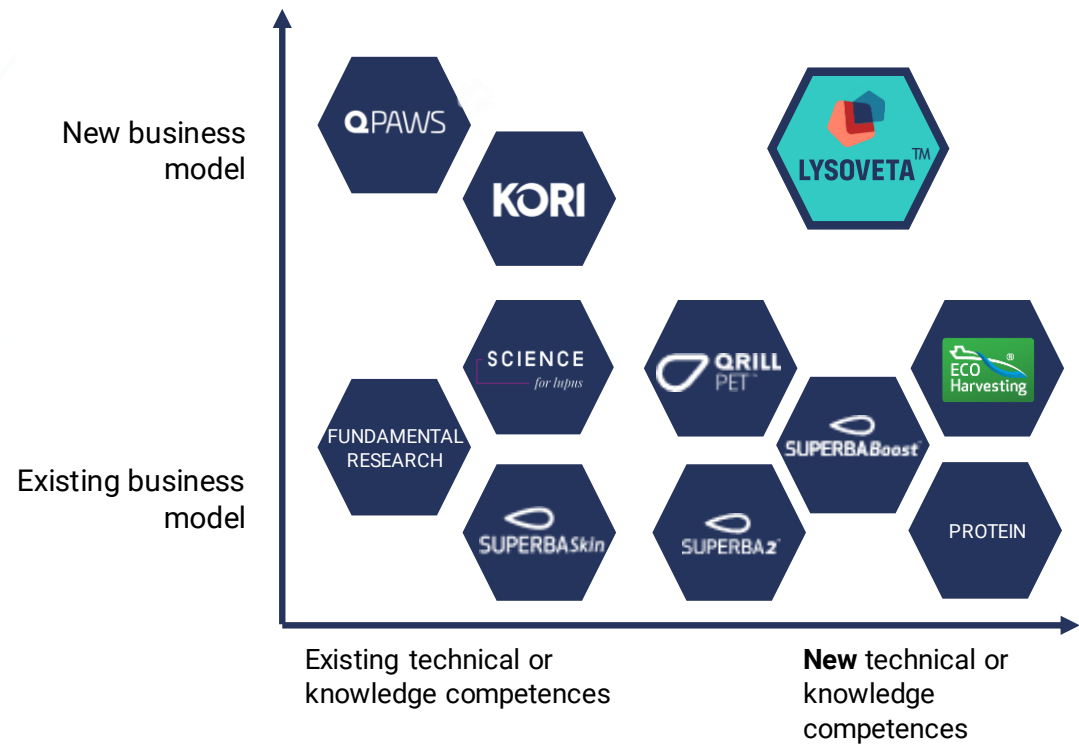
GLOBAL REVENUE BY SEGMENT



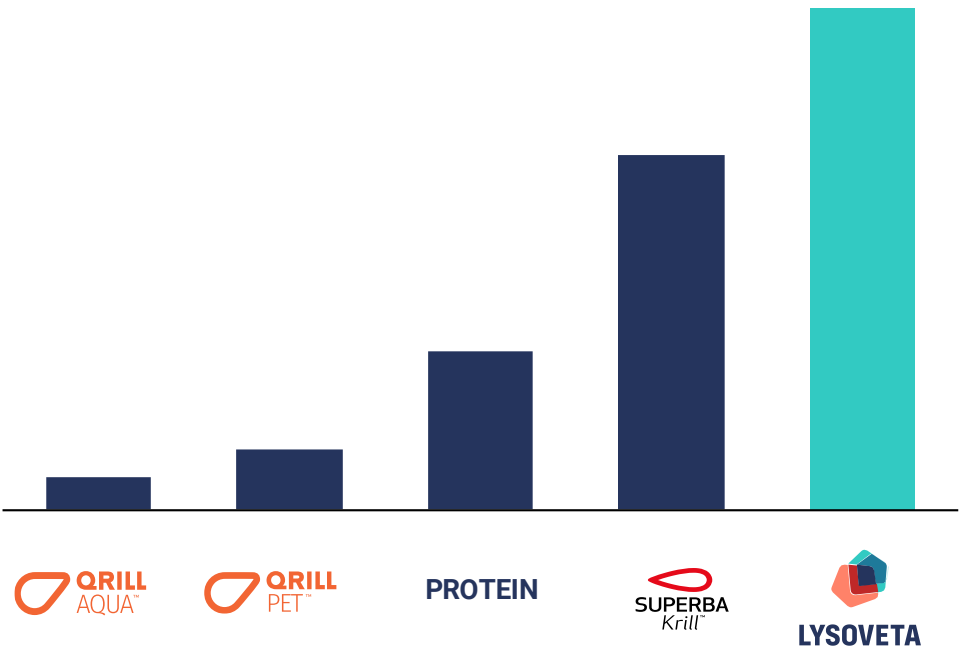
Source: Euromonitor – Health concerns with aging; Nielsen retail data, Evaluate Pharma – World Preview 2020, Outlook to 2026/World Preview 2019, Outlook 2019; Grand View Research, industry analysis eye health supplements/brain health supplements

THE NEW LYSOVETA™ BUSINESS WILL SIGNIFICANTLY LIFT PRODUCT PORTFOLIO MARGIN

WIDE RANGING INNOVATION COMPETENCIES...



...TARGETING SIGNIFICANT MARGIN UPLIFT POTENTIAL

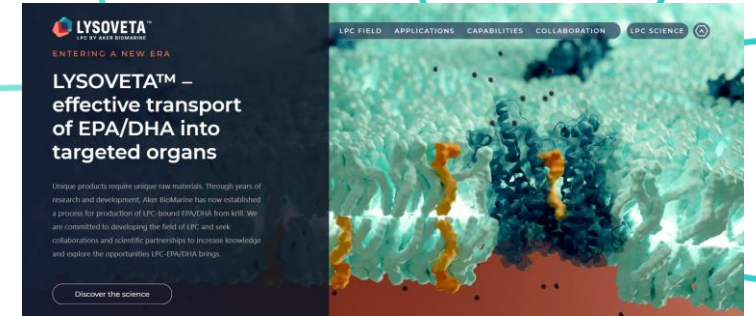


ROBUST COMPETITIVE ADVANTAGE FOR THE NEW BUSINESS AREA, LYSOVETA™ ENABLES AKER BIOMARINE TO CAPTURE THIS ATTRACTIVE SPACE

1.

FAST TRACK TO COMMERCIAL SUPPLEMENT PRODUCT

Commercialize LPC-DHA/EPA dietary supplement product and take to market by the end of 2022



2.

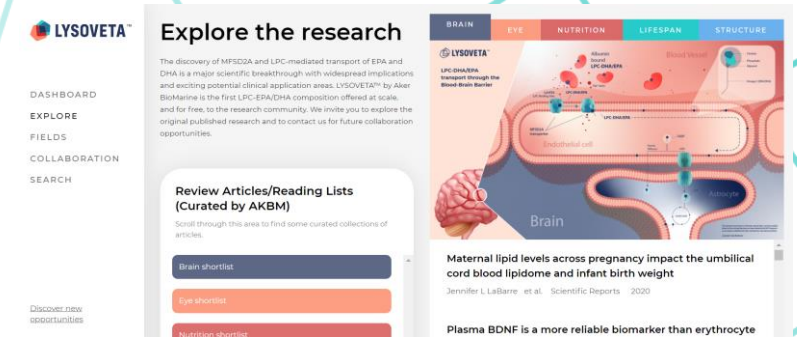
ESTABLISH COMMERCIAL PARTNERSHIPS

Reach out and work to establish commercial partnerships and collaborators to bring products to new segments (pharma, infant formula and functional foods..)

3.

DRIVE FURTHER RESEARCH AND DEVELOPMENT

Initiate and enable scientific community to drive further research and development in the LPC-DHA/EPA space



DEVELOPMENTAL AND NEUROLOGICAL DISORDERS CONSTITUTE A MAJOR CHALLENGE FOR PUBLIC HEALTH

Sustainability framework anchored in UN SDGs

Dedicated to improving human health




Promote mental health and well being



Pioneering sustainable fisheries



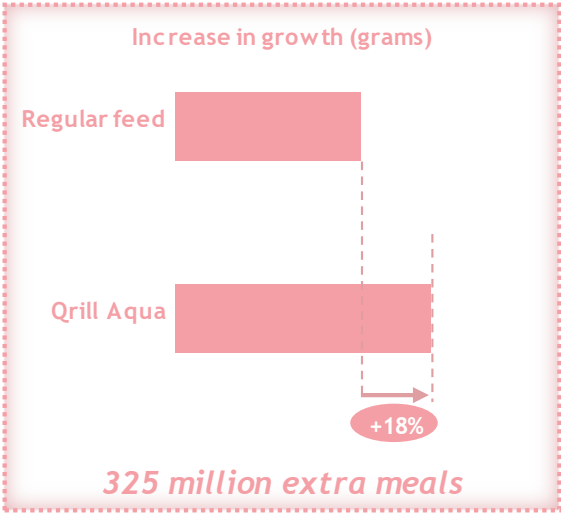
Highest ranking for sustainable fisheries

CERTIFIED SUSTAINABLE SEAFOOD MSC  www.msc.org			
MSC Principles	Fail (>60)	Best practice (60-80)	State of the art (80-100)
Sustainability of the stock	-	-	89
Ecosystem impacts	-	-	97
Effective management	-	-	96

Ingredients for more sustainable aquaculture



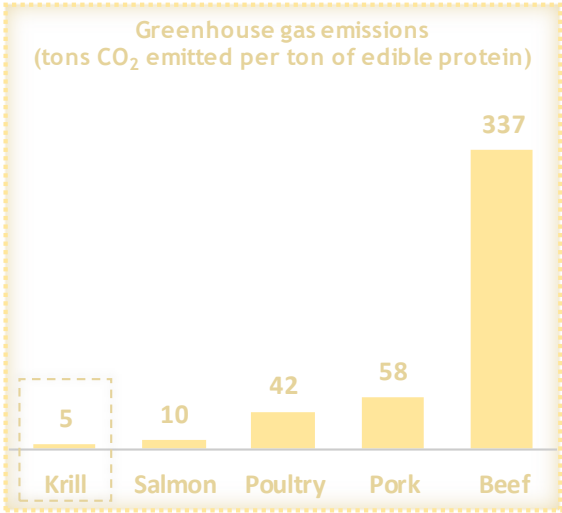
Increasing efficiency of aquaculture



Doing more and better with less



Reducing carbon emissions¹



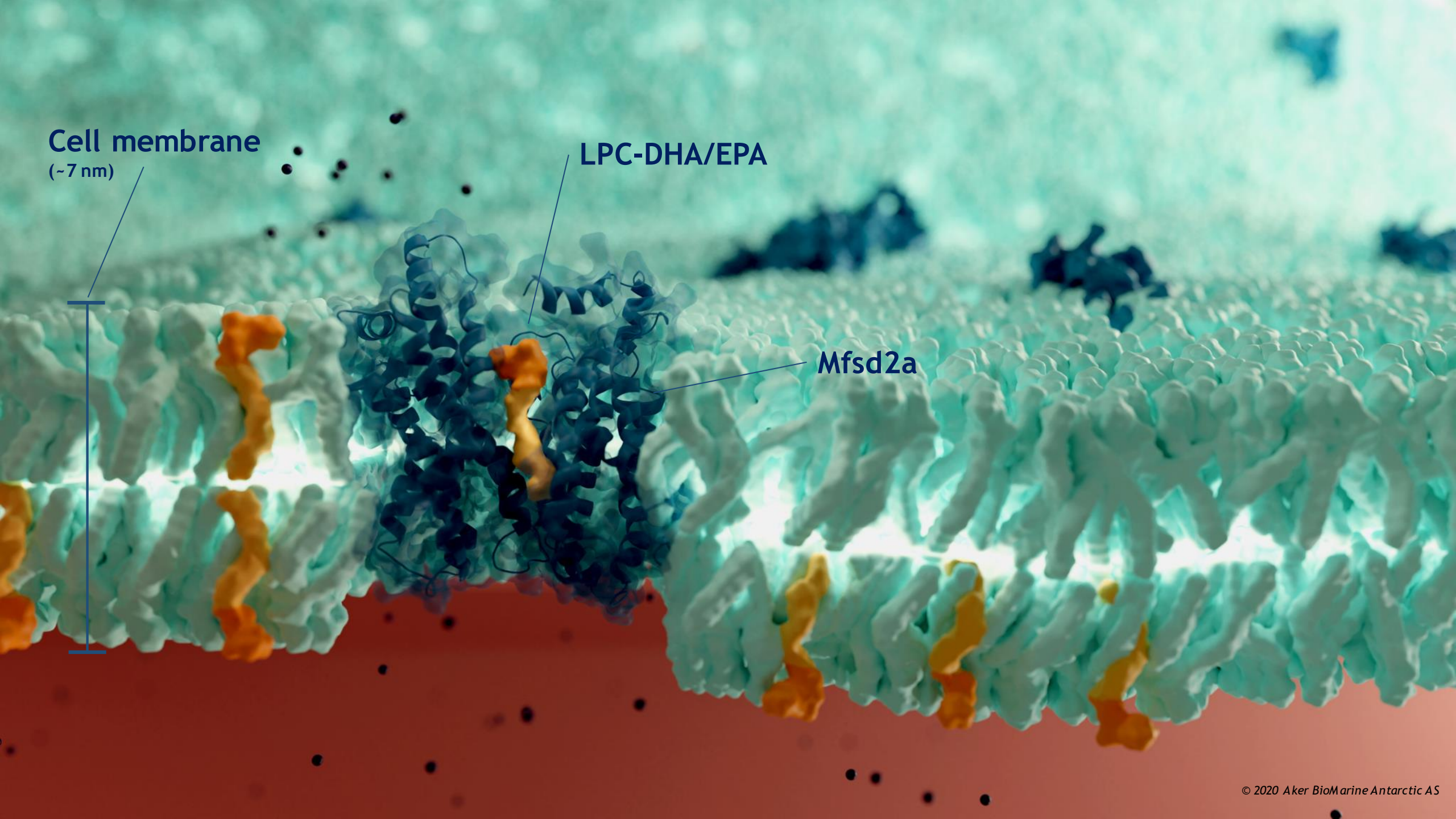
An undeterred focus on sustainability forms the bedrock of our growth strategy

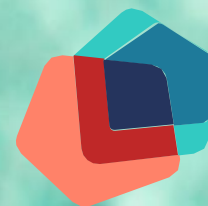
Source: Food supplements Europe “Healthcare Cost Savings of Omega 3 Food Supplements in the European Union”; Dalhousie University research 2011; Company data

Cell membrane
(~7 nm)

LPC-DHA/EPA

Mfsd2a





LYSOVETA

LPC-DHA/EPA

