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Beyond nutrition: lipids-based therapeutics from food and bioactive lipids

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Abstract

Lipid based therapeutics represent a clinically influential segment of the global pharmaceutical market and illustrate how the Food as Medicine concept can be translated into rigorously validated drugs. Lovaza/Omacor is a defining example: originally derived from a supplement grade omega-3 mixture, it progressed through large cardiovascular outcome trials such as GISSI Prevenzione and ultimately achieved full medicinal status, becoming the most commercially successful omega-3 drug worldwide. This trajectory is not unique. Retinoids and prostaglandin analogues show that lipid derived or nutrient related molecules can evolve into major therapeutic classes once they are purified, standardized, and clinically tested. Across fatty acids, prostaglandins, and retinoids, successful agents share clear mechanisms of action, controllable pharmacokinetics, and robust outcome level evidence—exemplified by icosapent ethyl and bempedoic acid in cardiovascular prevention, prostacyclins in pulmonary arterial hypertension, and retinoids in dermatology. By contrast, many investigational lipid compounds fail due to mechanistic ambiguity, safety liabilities, chemical instability, or poor regulatory fit. Cross-class analysis shows that lipid drugs succeed when their inherent biological promiscuity is constrained through formulation, structural refinement, and targeted delivery. Looking ahead, progress is expected from intravenous omega-3 emulsions, stable specialized pro resolving mediator analogues, next generation retinoids, and precision lipid modulators designed to harness endogenous signalling with greater specificity.

Keywords: Lipid-based therapeutics; Food-derived lipids; Bioactive lipids; Medicinal lipids.

1. Introduction

Contemporary public thought and current directions in food science strongly align with the idea that *"you are what you eat"* (WHO, 2026a; Lederer and Huber 2022; Drees and Barthel 2022; Landry et al., 2023) and with the broader Food-as-Medicine concept (Defraeye et al., 2025). Lipids constitute a major component of the human diet and play essential roles in nutrition, metabolism, and health. Yet public discourse often reduces this complexity to simplified categories—most notably the familiar distinction between "good" and "bad" fat—reflecting a tendency to classify dietary lipids as inherently healthy or unhealthy rather than as diverse bioactive molecules with context-dependent effects.

Together with proteins, nucleic acids, and polysaccharides, lipids constitute the fundamental structural and functional components of living systems, yet they remain among the most chemically and biologically diverse and least fully understood classes of biomolecules (Berg et al., 2023; Alberts, 2015). Although their roles in membrane architecture, energy storage, and cellular compartmentalization are well established, elucidating the precise biological functions and interaction networks of individual lipid species remains a major scientific challenge. Lipids participate virtually in all aspects of cellular physiology, including membrane dynamics, metabolic regulation, and signal transduction (Alberts, 2015; van Meer et al., 2008; Wenk, 2005).

Numerous classification schemes exist, reflecting the diversity of lipid structures and biosynthetic origins, but no single universally accepted definition has been adopted (Lipid Maps, 2026). A widely used structural description defines lipids as hydrophobic or amphipathic small molecules derived wholly or in part from carbanion-based condensations of thioesters and/or carbocation-

based condensations of isoprene units (Fahy et al., 2009).

New evidence on the benefits and risks of dietary fats is constantly evolving in both scientific literature and popular media, at times leading to significant controversy. This article reviews the exploitation of the intrinsic properties and health benefits of lipids, and their transformation into medicines designed to manage specific conditions (Zhang and Xu, 2025). As demonstrated in this review, while some lipid-based medicines have originated from foods, vitamins or dietary supplements, only a limited number of these transitions currently exist. Intrinsic hydrophobicity of lipids presents substantial challenges for their pharmaceutical development. Achieving selective intracellular delivery is difficult because many lipid species are rapidly metabolized by abundant endogenous enzymes such as lipases, phospholipases, and acyltransferases. Moreover, the chemical similarity of fatty acyl chains across lipid classes makes it difficult to design lipid-based therapeutics that interact with a single molecular target without nonspecific incorporation into cellular membranes, a phenomenon that can lead to off-target effects and toxicity (Flores et al., 2020; Luan et al., 2025).

The systemic administration of endogenous structural lipids such as omega-3 fatty acid esters, phospholipids, or cholesterol does not selectively modulate discrete biochemical pathways; instead, it broadly perturbs membrane composition, fluidity, and function, which can be deleterious. Likewise, many lipid-derived signalling mediators, including eicosanoids, sphingolipids, and lysophospholipids, exert highly localized, transient, and context-dependent effects (Hannun and Obeid, 2018). Delivering these molecules systemically risks triggering widespread and unpredictable downstream responses. Because fatty acids also serve as metabolic substrates, exogenous administration tends to expand general metabolic pools rather than produce targeted pharmacological actions. Despite these challenges, lipids remain central to disease biology and represent important therapeutic targets.

2. Therapeutics based on lipids and their derivatives

2.1. Lipid-based therapeutics excluded from this review

To maintain a focused scope and to prevent the discussion from being dominated by well-established steroid-based therapeutics, this article does not address drug products derived from steroids, including corticosteroids, estrogens and progestogens, vitamin D and its analogues, cardiac glycosides (steroidal but non-hormonal), steroidal antagonists and enzyme modulators, or bile acids and their derivatives. Likewise, isoprenoids, terpenes, and prenylated lipids fall outside the boundaries of this review.

The exclusion of these categories is purely a matter of scope; their medical and commercial importance is unequivocal. In fact, steroid-based and related lipid therapeutics constitute a substantial share of global pharmaceutical revenues.

Collectively, pharmaceutical products derived from steroids and other lipid categories excluded from this article generate an estimated USD 170 billion in annual global sales, with North America contributing approximately 30–50% of total revenues. These figures far exceed the commercial footprint of the lipid-based drug classes that are the focus of this article, namely fatty acids and their derivatives, prostaglandins, and retinoids (vitamin A derivatives).

2.2. Fatty acids and fatty acid derivatives

Fatty acid dietary supplements have become widely popular because they fill a nutritional gap that modern diets often leave open. Omega-3s, omega-6s, medium-chain triglycerides (MCTs), and other lipid ingredients play essential roles in cardiovascular health, inflammation balance, cognitive function, and cellular integrity, making them highly attractive to consumers focused on long-term wellness. Their popularity is also driven by strong clinical evidence for the benefits of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), growing interest in cardiovascular health, brain and metabolic health, and the rise of personalized nutrition. As a result, fatty acid supplements have moved from niche products to mainstream staples, supported by both healthcare practitioners and a global consumer base seeking simple, evidence-based ways to improve overall health. Some of them progressed towards medicine development as discussed in the sections below.

2.2.1. Short-chain and medium-chain saturated fatty acids and their derivatives

Drugs based on short-chain and medium-chain fatty acids (SCFAs/MCFAs) and their derivatives exploit the intrinsic metabolic, epigenetic, and signalling functions of simple fatty acids to modulate energy metabolism, inflammation, and cellular homeostasis. Pharmacologically, these agents act through diverse mechanisms, including histone deacetylase (HDAC) inhibition (e.g., sodium butyrate, valproate) (Davie, 2003; Chateauvieux et al., 2010), anaplerotic support of mitochondrial metabolism (e.g., triheptanoin) (Roe and Mochel, 2006), and targeted enzyme inhibition in lipid metabolism (e.g., bempedoic acid as an adenosine triphosphate (ATP)-citrate lyase inhibitor or etomoxir as a carnitine palmitoyltransferase-1 (CPT-1) inhibitor) (Pinkosky et al., 2016; Lopaschuk et al.,1994). Drug development has focused on improving bioavailability, tissue targeting, and safety through prodrug strategies, salt forms, and structural modification of native fatty acids. Clinically, several SCFA/MCFA-derived drugs are well established in neurology, rare metabolic diseases, and cardiometabolic indications. Others remain important research tools or investigational agents, underscoring this class as a small but mechanistically diverse and clinically validated category of lipid-derived therapeutics.

2.2.1.1. Sodium butyrate

Sodium butyrate (Figure 1) is a common component of the human diet, produced in large amounts from dietary fibre in the gut and present in foods such as Parmesan cheese and butter (RSC, 2026). Although not yet an approved therapeutic drug, sodium butyrate is an active investigational compound currently being explored across multiple clinical research programs and trials, including studies in immunology, neurology, and metabolic health (NIH, 2026a). Conditions under investigation include rheumatoid arthritis, graft-versus-host disease, hypertension, chronic mesenteric ischemia, and cognitive function in schizophrenia. The compound is also being explored as a histone deacetylase inhibitor for neurological and psychiatric disorders such as Alzheimer's, Parkinson's, and Huntington's disease (Rahmani et al., 2025). Sodium butyrate has an official orphan designation in the EU for the treatment of radiation proctitis (Vernia et al., 2000).

2.2.1.2. Valproate

Valproate was first introduced as a medication in 1962; however, its precise mechanism of action remains unclear. Proposed mechanisms

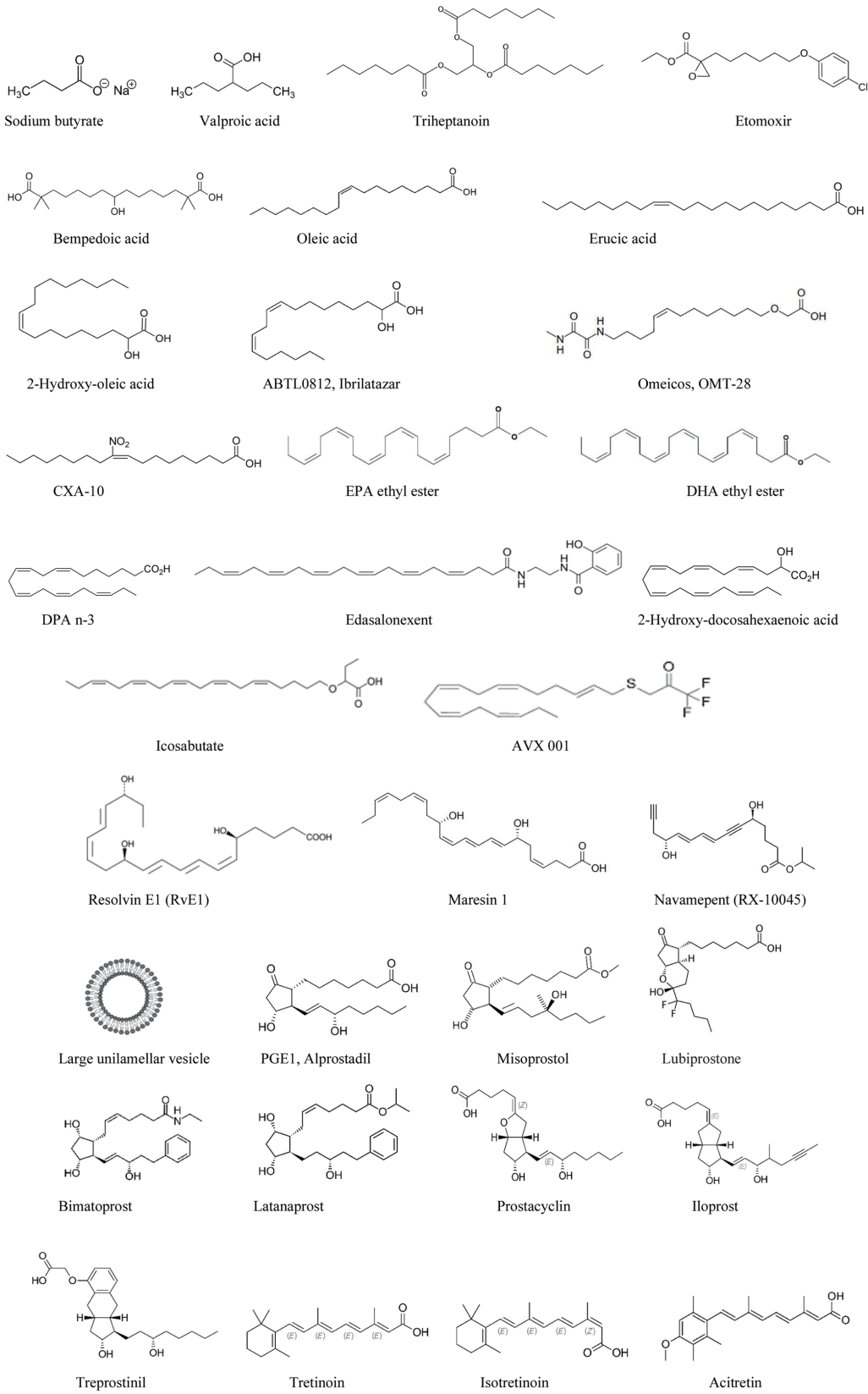

Figure 1. The chemical structures of all therapeutics and main relevant compounds listed in the article.

include modulation of gamma-aminobutyric acid (GABA) levels, blocking of voltage-gated sodium channels, inhibition of histone deacetylases, and enhancement of lymphoid enhancer factor 1 (LEF1) (Drugs, 2026a; Ghodke-Puranik et al., 2013; Santos et al., 2021).

Valproic acid (Figure 1) and its sodium forms are medications primarily used to prevent migraine headaches, and to treat epilepsy and bipolar disorder (Drugs, 2026a). Due to its histone-deacetylase-inhibiting effects, the medication has also been tested in the treatment of AIDS and cancer. Valproic acid is recognized for its cardioprotective, kidney-protective, and anti-inflammatory properties, and it also exhibits antimicrobial effects (Singh et al., 2021). It is currently included on the World Health Organization's List of Essential Medicines. The medicine is approved in various forms by the US FDA, Health Canada (under the brand names Depakene®, Epival®, and Epiject®), and the EMA (US FDA, 2026a; EMA, 2026a).

2.2.1.3. Triheptanoin

Triheptanoin (Figure 1, Dojolvi®, Ultragenyx®) is a medication approved by the FDA for treating children and adults with confirmed long-chain fatty acid oxidation disorders (LC-FAODs) (US FDA, 2026b). The odd-carbon fatty acids function by providing anaplerotic substrates for the tricarboxylic acid (TCA) cycle (Mochel et al., 2005). Approved for medical use in the United States in June 2020 (Shirley, 2020), triheptanoin is used clinically to treat inherited metabolic diseases, such as pyruvate carboxylase deficiency and carnitine palmitoyltransferase II deficiency (Roe et al., 2008). Additionally, it appears to enhance the efficacy of the ketogenic diet in treating epilepsy (Avila et al., 2023).

2.2.1.4. Etomoxir

Originally developed as a metabolic therapy for conditions such as type 2 diabetes and heart failure, etomoxir (Figure 1, Numiera Therapeutics) is an investigational drug originating from Germany (Amschler et al.,1983). It is a uniquely derivatized ethyl ester of 2,8-dihydroxy-octanoic acid. In the form of the dextrorotatory (R)-(+)-enantiomer, this compound is an irreversible inhibitor of CPT-1 located on the inner face of the outer mitochondrial membrane (Kruszynska and Sherratt, 1987). Etomoxir prevents the formation of acyl carnitines, a step that is necessary for the transport of fatty acyl chains from the cytosol into the intermembrane space of the mitochondria. This step is essential to the production of adenosine triphosphate (ATP) from fatty acid oxidation. Etomoxir has also been identified as a direct agonist of peroxisome proliferator-activated receptor alpha (PPARα) (Cheng et al., 2019).

In 2025, Numiera Therapeutics secured orphan drug designation for etomoxir for the treatment of malignant glioma, and the company plans to conduct trials in neuro-oncology (Dominiak et al., 2025). Despite its long scientific history, etomoxir remains investigational, lacking marketing authorization, due in part to concerns about off-target effects that were uncovered during earlier clinical development.

2.2.1.5. Bempedoic acid

Bempedoic acid (Figure 1, Nexletol®, Nilemdo®, Esperion Therapeutics) is a synthetic compound generated by bridging two molecules of ethyl 7-bromo-2,2′-dimethyl-heptanoate via the carbon atom donated by toluenesulfonyl isocyanide (tosMIC) (Oniciu and Dasseux, 2004). It is not a fatty acid molecule found in lipids, but rather a molecule based on a dicarboxylated linear C15 hydrocarbon chain core like thapsic acid (C16). It is a medication for hypercholesterolemia, typically administered as an adjunct to diet in combination with a statin in patients unable to reach low-density lipoprotein cholesterol (LDL-C) goals or in patients who are statin intolerant. It blocks ATP-citrate lyase, involved in the biosynthesis of cholesterol in the liver, upstream of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the target of statins (Paton, 2017). Bempedoic acid was approved by the US FDA in February 2020 as a first-in-class medication and by the EMA in April 2020 (EMA, 2026b; US FDA, 2026c). The FDA approved bempedoic acid based on results from two clinical trials (Trial 1/NCT02666664 and Trial 2/NCT02991118) that involved more than 3,000 subjects with high LDL cholesterol and known atherosclerotic cardiovascular disease or heterozygous familial hypercholesterolemia. The trials were conducted in the United States, Canada, and Europe (US FDA, 2026d). Health Canada approved the drug in November 2025 (Cision Canada, 2026).

2.2.2. Long-chain mono-unsaturated and di-unsaturated fatty acids and their derivatives

Drugs based on long-chain monounsaturated and di-unsaturated fatty acids (LCMUFAs and LCDUFAs) aim to harness lipid signalling and membrane-modulating effects—such as altering membrane structure and receptor function, shifting inflammatory lipid mediator profiles, and engaging lipid-sensing transcription factors—to treat metabolic dysfunction, inflammatory, mitochondrial and neurodegenerative diseases, cardiovascular disease and cancer (Scott et al., 2022; Hashimoto and Hossain, 2018; Toncan et al., 2025; Tsutsumi et al., 2021; Pedersen et al., 2025). Development has emphasized chemically defined fatty-acid derivatives and stabilized analogs (e.g., hydroxylated or otherwise functionalized oleic/linoleic-type scaffolds) to improve potency, selectivity, and pharmacokinetics compared with dietary lipids. Clinically, only a small number of such molecules have progressed to human trials, and none has become broadly established as a mainstream small-molecule "fatty-acid drug" class; however, several candidates remain in development as first-in-class therapies that exploit unique membrane and immunometabolic mechanisms distinct from conventional anti-inflammatories.

2.2.2.1. Lorenzo's oil

The 1992 film Lorenzo's Oil brought significant public attention to a triglyceride mixture used to treat adrenoleukodystrophy (ALD) (Hudson Jones, 2000). Named after Lorenzo Odone, the main character in the film who had ALD, the oil consists of glyceryl trierucate and glyceryl trioleate in an approximate 1:4 ratio.

ALD and adrenomyeloneuropathy (AMN) are rare genetic disorders characterized by a buildup of very long-chain fatty acids, which can cause serious neurological and physical complications. While Lorenzo's oil is commonly used for these conditions, there is currently a lack of strong scientific evidence to support many of its applications. Consequently, in the United States, this oil is only available to patients enrolled in clinical trials (NIH, 2026b, 2026c).

2.2.2.2. LAM 561

LAM 561 (Figure 1, 2-hydroxy-oleic acid, Minerval®, Laminar

Pharma) is an experimental oral anticancer agent that targets tumour cell membrane lipid composition (membrane lipid therapy) (Laminar Pharma; Adam et al.,1998; Escriba-Ruiz et al., 2013). It is designed to disrupt signalling pathways essential for cancer cell proliferation, particularly in glioblastoma (Torgersen et al., 2016). It reached the Phase IIb/III CLINGLIO trial in adults with newly diagnosed, IDH-wildtype glioblastoma. The results imply that adding LAM561 to standard combination of radiotherapy and temozolomide may delay disease progression in patients whose tumours exhibit O-6-methylguanine-DNA methyltransferase (MGMT) promoter methylation (Rare Cancer News, 2026; NIH, 2026d). While promising, these findings are preliminary, particularly outside the methylated subgroup, and definitive efficacy and regulatory conclusions will rely on completion of the trial and final survival outcomes (Rare Cancer News, 2026; PR Newswire, 2026a).

2.2.2.3. Ibrilatazar

Ibrilatazar (ABTL0812, 2-hydroxy-linoleic acid, Figure 1) is an investigational drug developed by Ability Pharmaceuticals (Escriba-Ruiz et al., 2013). In 2015, the company received orphan drug designation (ODD) for pediatric neuroblastoma from the EMA and the US FDA , and in December 2016, the company announced that ibrilatazar had received an ODD for the treatment of pancreatic cancer (PR Newswire, 2026b). The compound is under investigation in clinical trial NCT04431258 in combination with FOLFIRINOX (a chemotherapy regimen for treatment of advanced pancreatic cancer) (DrugBank, 2026a). Ibrilatazar combined with paclitaxel and carboplatin was also tested in the treatment of several cancers, and demonstrated promising efficacy and safety in advanced squamous non-small cell lung cancer (sq-NSCLC) (Bosch-Barrera et al., 2025). Ibrilatazar activates PPARα and PPARγ, which subsequently increase tribbles pseudokinase 3 (TRIB3) expression. However, recently, the proposed mechanism of action of ibrilatazar has raised important questions (Rosell, 2025).

2.2.2.4. OMT-28

OMT-28 (Figure 1) is a synthetic molecule, selected from a portfolio of patented derivatives developed by Omeicos Therapeutics, a spin-off from the Max Delbrück Center for Molecular Medicine in Berlin. The compound is designed to modulate inflammation and mitochondrial dysfunction in diseases with significant unmet need. OMT-28 is a metabolically robust molecule designed to mimic the structure and function of omega-3 epoxyeicosanoids (Adebesin et al., 2019).

OMT-28 was engineered to capture the cardioprotective and mitochondria-stabilizing activities of endogenous electrophilic lipid mediators. It has undergone clinical evaluation in atrial fibrillation (AF) and is now being advanced for primary mitochondrial disease (PMD). In the completed PROMISE-AF Phase II trial, OMT-28 was assessed as a once-daily therapy to maintain sinus rhythm following electrical cardioversion in patients with persistent AF (Berlin et al., 2020; In Clinical Trials, 2026). Later, Omeicos completed enrollment in the PMD OPTION Phase IIa study, with interim analyses demonstrating a favourable safety profile, good tolerability, and encouraging pharmacodynamic responses in PMD patients presenting with myopathy or cardiomyopathy (ICH GCP, 2024). Together, these results highlight OMT-28's promise as a novel therapeutic targeting mitochondrial dysfunction and inflammation.

2.2.2.5. CXA-10

CXA-10 (10-nitro-oleic acid, Figure 1, Complexa Inc.) is the most clinically advanced member of the nitro-fatty acid class (Woodcock et al., 2013; Koutoulogenis and Kokotos, 2021). It is currently being evaluated in Phase I/II studies for inflammatory and fibrotic disorders, including focal segmental glomerulosclerosis and pulmonary arterial hypertension (NIH, 2026e). CXA-10 acts through reversible alkylation of cysteine residues on key regulatory proteins, thereby activating cytoprotective pathways—most notably nuclear factor erythroid 2-related factor 2 (Nrf2)—while suppressing pro-inflammatory signalling such as nuclear factor kappa B (NF-κB) (Gao et al., 2022).

Other nitro-fatty acids, including nitro-linoleic acid and various synthetic analogues, have demonstrated anti-inflammatory, antioxidant, and cytoprotective properties in preclinical models, though most remain in early development. Collectively, this class offers a distinctive therapeutic strategy that leverages endogenous lipid-signalling mechanisms to counter inflammation, oxidative stress, and related pathologies. Nitro-fatty acids are emerging as promising candidates for various conditions, primarily for chronic inflammatory diseases and cancer (Schopfer et al., 2018; Roos et al., 2024).

2.2.3. Drugs developed from fish oil and omega-3 derivatives

Fish oil and omega-3-derived drugs translate the biological activities of EPA and DHA—particularly triglyceride lowering, modulation of membrane composition, and downstream effects on inflammatory and thrombotic signalling—into standardized, pharmaceutical-grade products with defined dosing and quality (Kawasaki et al., 2019; Skulas-Ray et al., 2019). The development progressed from mixed omega-3 ethyl ester concentrates to purified single-entity agents and novel derivatives designed for greater potency, consistency, and improved cardiometabolic risk modification (Fialkow, 2016; Hilleman et al., 2020). Clinically, omega-3 drugs are firmly established for severe hypertriglyceridemia with ongoing debate and research on their cardiovascular outcomes depending on formulation, dose, and patient population (Skulas-Ray et al., 2019; US Pharmacist, 2026; Kapoor et al., 2021). Current pipelines also include more specialized omega-3 derivatives (including prodrug approaches and mediator-inspired analogs) aimed at extending benefits beyond lipids into inflammation-driven diseases.

2.2.3.1. Omega-3 fatty acid products with free or substituted carboxyl groups

This review does not seek to revisit the health benefits of omega–3 fatty acids, a topic already examined in extraordinary depth. An excellent source of information related to omega-3s is The Global Organization for EPA and DHA Omega-3s (GOED). As stated on their website, "*GOED's purpose is to be the omega-3 industry advocate and knowledge hub*" and indeed, it is an outstanding resource and actionable guidance on omega-3s. Also, recent publications provide comprehensive reviews of this busy field (Patted et al., 2024; Wang et al., 2024; Saidaiah et al., 2024), and a bibliometric analysis using the Web of Science identified 18,764 omega-3-related research articles published between 2014 and 2023 alone (Wang et al., 2024). Instead, the purpose of this section is to highlight the major omega-3-based medicines approved by regulatory agencies, along with key compounds that have undergone or are currently undergoing clinical investigation.

2.2.3.1.1. Icosapent ethyl

Icosapent ethyl (Figure 1, a 96% ethyl ester of EPA) was originally developed in Japan by Mochida under the name Epadel® and approved for the Japanese market in 1990 (PMDA, 2020). This occurred well before omega-3 dietary supplements gained popularity in the United States and more than a decade before the first omega-3 pharmaceutical products—Omacor® in Europe and Lovaza® in the US—were approved. Epadel® formulation was developed for lowering elevated serum triglycerides and the treatment of arteriosclerosis obliterans. Epadel® was supported by the large JELIS trial, which enrolled 18,645 patients on low-dose statins and demonstrated that adding 1,800 mg/day of EPA produced a 19% relative reduction in major coronary events over 4.6 years, with an even greater 21% reduction in secondary-prevention patients with established coronary artery disease (Yokoyama et al., 2007).

While Epadel® was first developed and marketed in Japan, Vascepa® was later developed by Amarin and approved in the United States and other global markets. In contrast, Vascepa®'s global development followed a stepwise program beginning with the MARINE trial (Bays et al., 2011), which showed that 4 g/day of icosapent ethyl reduced triglycerides by 33% in severe hypertriglyceridemia without raising LDL cholesterol, leading to its initial FDA approval in 2012 (PR Newswire, 2026c). The subsequent ANCHOR trial (Ballantyne et al., 2012) confirmed triglyceride lowering in statin-treated patients with moderately elevated triglycerides. However, it did not prompt an immediate label expansion due to the absence of outcomes data. Definitive evidence arrived with the REDUCE-IT trial (Bhatt et al., 2019; Harris, 2019), an 8,179-patient cardiovascular outcomes study showing a 25% reduction in major adverse cardiovascular events in high-risk statin-treated patients, which secured Vascepa®'s 2019 approval for cardiovascular risk reduction and established it as a major therapeutic advance in omega-3 pharmacotherapy (PR Newswire, 2026c).

Although Epadel® and Vascepa® share EPA as their core component, differences in regulatory pathways and clinical evidence requirements have resulted in divergent positioning and approved uses across markets. Amarin remains the sole developer and marketer of branded Vascepa® in the US and Vazkepa® in the EU and other regions. In the US market, major generic manufacturers include Apotex, Hikma, Dr. Reddy's, Teva, Amneal, Zydus, Strides, and Puracap, alongside numerous additional producers globally, particularly in China.

2.2.3.1.2. Omacor® (Lovaza®)

Omacor®, in the US under the name Lovaza®, is widely regarded as a clear example of how evidence generated with a highly purified dietary supplement can be translated into a licensed cardiovascular medicine. Its development pathway is unusual in modern drug history: the pivotal evidence base was established not through a traditional investigational new drug program, but through large, pragmatic cardiovascular outcome trials that used the same omega-3 ethyl ester formulation later commercialized as a prescription product. Regulatory authorities in Europe explicitly acknowledged this trajectory, noting that Omacor®'s original approval for secondary prevention after myocardial infarction was based on the open-label GISSI-Prevenzione study (GISSI, 1999), which used the identical omega-3 acid ethyl ester preparation later marketed as the medicinal product. This made Omacor®/Lovaza® one of the rare cases in which a supplement-grade formulation—once subjected to rigorous, large-scale clinical evaluation—demonstrated sufficient efficacy and safety to justify full medicinal authorization.

The GISSI-Prevenzione trial enrolled 11,324 recent myocardial infarction (MI) survivors across Italy and randomized them to 1 g/day of omega-3 ethyl esters, vitamin E, both, or neither. Omega-3 treatment produced a 10–15% reduction in the composite endpoint of death, non-fatal MI, and stroke, with no benefit from vitamin E alone. The most influential finding was a ~45% reduction in sudden cardiac death and a ~20% reduction in total mortality, establishing the first large-scale "real-world" evidence that purified omega-3 ethyl esters could improve survival in post-MI patients. These results directly supported Omacor®'s regulatory approval for secondary prevention. The latter GISSI-HF trial extended this evidence by showing that the same 1 g/day dose reduced mortality and hospitalizations in chronic heart failure (Tavazzi et al., 2004), reinforcing the clinical relevance of the formulation across broader cardiovascular populations.

Lovaza® is a concentrated mixture of fish-oil-derived ethyl esters formulated in one-gram soft-gel capsules containing approximately 465 mg of EPA ethyl ester and 375 mg of DHA ethyl ester, yielding more than 900 mg of total omega-3 ethyl esters (Figure 1) per capsule (Lovaza, 2026; Drugs, 2026b). Originally developed and introduced by Pronova as Omacor®, it received EMA approval in 1999 and FDA approval in 2004.

A related product, Omtrygg® (Trygg Pharma), contained the same amounts of EPA, DHA, and total omega-3s but was delivered in a larger 1.2-g capsule; this formulation has since been discontinued. Another formulation, Hepacor®, from Ideogen (originally manufactured by BASF) provides a Lovaza-based composition in a 750-mg capsule; however, it is marketed as a food supplement for special medical purposes rather than as a prescription drug. Do not confuse with the medication manufactured by Intas Pharmaceuticals that shares the same name. While both products are used to manage metabolic dysfunction-associated steatohepatitis (MASH), the product manufactured by Intas is not based on omega-3s but on L-ornithine-L-aspartate.

Lovaza® has also distinguished itself as the most commercially successful omega-3 prescription product to date, achieving market penetration and revenue levels unmatched by later entrants. Across multiple market analyses, Lovaza® is consistently listed alongside Vascepa® as one of the two dominant products in the global omega-3 prescription segment, with Lovaza® maintaining a leading position for more than a decade after its launch. Reports covering the period from the mid-2000s through the 2020s show that Lovaza® remained a core revenue driver within the omega-3 drug class, contributing substantially to a global market valued at approximately USD 1.40 billion in 2024 (Grand View Research, 2026), with Lovaza® occupying a major share of this space. This sustained performance reflects not only early regulatory approval and first-mover advantage but also broad clinical adoption for hypertriglyceridemia management, supported by extensive post-marketing experience and physician familiarity. Even as newer formulations entered the market, Lovaza®'s established safety profile, widespread insurance coverage, and strong brand recognition allowed it to retain a dominant commercial footprint. Market reports continue to classify Lovaza® as one of the principal contributors to global omega-3 prescription drug revenues, underscoring its long-standing status as the most successful omega-3 ethyl ester formulation in the pharmaceutical sector.

2.2.3.1.3. Epanova®

Epanova® was initially developed by Ocean Nutrition Canada

Table 1. Orally administered omega-3 prescription medicines and food supplements for special medical purposes

Name	Brand/Other Names	Origin/ Developer	Current Manufacturer	Regulatory Approval	Main Indication	Other Indications	Composition	Notes
Eicosapentaenoic acid ethyl ester (EPA-EE)	Epadel® Vascepa® Vazkepa®	Mochida	Amarin	FDA 2013; expanded 2019; Japan 1990	HTG, AO	HT, DM, PC	EPA-EE 97%	OTC in Japan since 2013 (EPADEL-T®, Taisho)
Omega-3-acid ethyl esters	Omacor® Lovaza®	Pronova	GSK	FDA 2004; EMA 1999	HTG	DL	EPA 465 mg, DHA 375 mg (900 mg ω-3/1 g capsule)	Four FDA-approved generics (as of 03/2016)
Omega-3-acid ethyl esters	Omtryg®	Pronova	Trygg Pharma	FDA 2004; national authorizations in EU	Severe HTG	–	EPA 465 mg, DHA 375 mg (900 mg ω-3/1.2 g capsule)	Discontinued
Omega-3-acid ethyl esters	Hepacor®	BASF (Pronova)	Ideogen	Not FDA-approved; not a drug	NAFLD	–	Lovaza-equivalent composition in 750 mg capsule	Food supplement for special medical purposes
Omega-3-carboxylic acids (free fatty acids)	Omefas Epanova®	Tillotts/ ONC	AstraZeneca	FDA 2014	Severe HTG	–	5520 mg ω-3 FFA	Discontinued

AO, arteriosclerosis obliterans; DL, dyslipidemia; DM, diabetes mellitus; HT, hypothyroidism; HTG, hypertriglyceridemia; NAFLD, non-alcoholic fatty liver disease; OTC, over the counter; PC, pancreatitis.

(ONC) for Tillotts Pharma. It was subsequently acquired by AstraZeneca through Omthera Pharmaceuticals. The product contains a 50/20 EPA/DHA mixture formulated as free fatty acids rather than ethyl esters, distinguishing it from products such as Lovaza® and Vascepa®. Development was discontinued after the STRENGTH trial, a large Phase III cardiovascular outcomes study, failed to demonstrate a reduction in major adverse cardiovascular events when Epanova® was administered in combination with statins. The trial enrolled more than 13,000 patients across 22 countries, but outcomes did not differ significantly from placebo (Nichols et al., 2020).

2.2.3.1.4. Alfa (EPAspire™)

Alfa (EPAspire™) is a product developed by KD Pharma and SLA Pharma. It is a highly purified EPA in free fatty acid form mixed with a sweet wormwood (*Artemisia annua*) extract in a gastro-resistant capsule, and it is an investigational drug in clinical trials in Europe. The primary indication is familial adenomatous polyposis (FAP)—a rare genetic condition linked to colorectal cancer risk (West et al., 2010). Currently, it is in Phase III trials for FAP across multiple countries (NIH, 2026f). The secondary indication is a COVID-19-related inflammation, and trials were initiated to explore its potential in reducing progression to severe outcomes such as acute respiratory distress syndrome and intensive care unit admission (NIH, 2026g). EPAspire™ is believed to suppress inflammatory cytokines, which may help mitigate disease progression in both FAP and COVID-19 contexts (Montemarano, 2020). It is approved for clinical trials by the UK's MHRA, and applications have been submitted to other European authorities and the US FDA.

2.2.3.1.5. Lypdiso™ (MAT9001)

Lypdiso™ (MAT9001, Matinas BioPharma) is an investigational omega-3 free fatty acid-based composition (a patented proprietary combination of a sizable dose of EPA, low amounts of DHA and the addition of DPA, docosapentaenoic acid n-3, Figure 1) developed for cardiovascular and metabolic conditions with a focus on triglyceride lowering. Early comparative studies (e.g., ENHANCE-IT) vs Vascepa® demonstrated increased EPA levels and trends toward improved serum lipid levels, although not all outcomes reached statistical significance (NIH, 2026h; Maki et al., 2022). Unfortunately, there are limited recent publicly available data on further clinical advancement; the status appears unchanged, with no new large-scale trials actively reported.

All US FDA/EMA-approved EPA/DHA-derived medicines are summarized in the Table 1. These are all ethyl esters except for Epanova® that failed to reach the market due to its failure in the major clinical trial. The investigational drugs described below and in the following two sections (2.2.3.2 and 2.2.3.3) are omega-3-based but display greater structural versatility.

2.2.3.1.6. Edasalonexent

Edasalonexent (CAT-1004, Figure 1, Catabasis Pharmaceuticals/ Astria Therapeutics) is a salicyl hydrazide derivative of DHA and an investigational oral inhibitor of NF-κB. Early clinical studies in Duchenne muscular dystrophy (DMD) showed promising results, with Phase II data indicating slowed disease progression and preservation of muscle function (Finanger et al., 2019). These encouraging findings sparked the initiation of the global Phase III PolarisDMD trial to evaluate efficacy and safety for potential regulatory approval. However, clinical registry summaries of the Phase III study (NCT03703882) are with mixed interpretations (NIH 2026i; Finkel et al., 2021). The data were inconclusive, and the trial did not reach statistical significance on its primary functional endpoints, although subgroup analyses suggested potential benefit in younger patients. Development was further supported by orphan drug and rare pediatric disease designations (Muscular Dystrophy News, 2026).

2.2.3.2. Omega-3 derivatives with C-2 substitution

2.2.3.2.1. LAM 226

LAM 226 (2-hydroxy-docosahexaenoic acid, Figure 1) is an investigational DHA derivative under development by Laminar Pharmaceuticals for neurodegenerative diseases, including Alzheimer's disease. The molecule is designed to leverage omega-3-specific transport pathways in neuronal membranes. Preclinical *in vitro* and in *vivo studies* indicate that LAM 226 reduces tau hyperphosphorylation, a core pathological hallmark of Alzheimer's. Reported benefits also include improved performance in rodent cognitive-behaviour assays, reduced β-amyloid burden, and restoration of key synaptic proteins in the hippocampus, such as synaptophysin and synaptosome-associated protein SNAP-25 (Mohaibes et al., 2017).

Despite these promising findings, LAM 226 remains at the preclinical stage, with no human trials reported to date. Nevertheless, its strong efficacy signals in rodent models support continued exploration as a potential disease-modifying therapy for Alzheimer's disease and related tauopathies (Parets et al., 2020).

Other hydroxy-DHA derivatives, including 4-HDoHE, 10-HDoHE, and DHA-derived fatty-acid esters of hydroxylated fatty acids (FAHFAs), have likewise shown intriguing biological activities in preclinical systems. However, apart from LAM 226, none are currently recognized as formal investigational drug candidates in clinical development.

2.2.3.3. Other PUFA derivatives

2.2.3.3.1. Icosabutate

Icosabutate (Figure 1) is an ether formed from eicosapentaenol and 2-hydroxybutyrate, engineered to resist the metabolic breakdown of EPA as an energy substrate, thereby enabling direct pharmacological action on hepatic inflammation and fibrosis. Designed as a liver-targeted agent, it activates free fatty acid receptors FFAR1 and FFAR4 and exhibits anti-inflammatory and anti-fibrotic effects that are independent of weight loss or reductions in liver fat. The compound has completed the Phase IIb ICONA trial for MASH (Harrison et al., 2025) and is now progressing toward registrational clinical development, with plans underway to initiate pivotal trials.

2.2.3.3.2. AVX 001

AVX-001 (Figure 1, AKH-217, Coegin Pharma AB; formerly Coegin/Coexxin AS) is a cytosolic phospholipase A_2 inhibitor that was initially explored as a potential treatment for psoriasis, actinic keratosis, and basal cell carcinoma (NIH, 2026j; Ortner et al., 2022). Following early-stage clinical investigations, development activity has largely stalled, with no recent clinical trials or regulatory submissions publicly reported.

Table 1 summarizes all orally administered omega-3 drugs approved by the US FDA or the EMA. Only two omega-3 oral drugs—Lovaza® and Vascepa®—have reached approval despite a crowded pipeline, underscoring how difficult it is for new candidates to demonstrate clinically meaningful, regulator-acceptable benefits. Many investigational products struggle with inconsistent cardiovascular outcomes, formulation challenges, or safety and purity concerns that limit advancement. This contrast highlights a translational bottleneck: while omega-3 biology is promising, turning it into reliable, scalable therapeutics remains far more complex than early mechanistic data suggest.

2.2.3.4. Parenterally administered omega-3 therapeutics

2.2.3.4.1. Omegaven®

Omegaven® is a 10% fish-oil emulsion containing 13–26% EPA and 14–27% DHA in the form of triacylglycerols within the oil phase. It is manufactured by Fresenius Kabi, and it received regulatory approval in the EU in 1998 and from the US FDA in July 2018 (Fresenius, 2026). In Canada, access is limited to Health Canada's Special Access Program. The formulation supplies calories and essential fatty acids for pediatric patients with parenteral-nutrition-associated cholestasis (PNAC), including newborns with very low birth weight, gastroschisis, or intestinal atresia (Christensen et al., 2007). It is administered as part of total parenteral nutrition (TPN), for example, in cases of short bowel syndrome (Gura et al., 2006).

Omegaven® was introduced as an alternative to Intralipid®, a product based on soybean-oil emulsions (10%, 20%, or 30%), first marketed in Sweden in 1962, and approved by the US FDA in 1972. Transitioning from Intralipid® to Omegaven® was associated with a reduced risk of liver injury (Mayser et al., 2002). Additional clinical observations reported improvements in psoriasis compared with Lipoven® (20% soybean oil) (Mayser et al., 2002), and reductions in mortality and antibiotic use during hospitalization. A comprehensive review of omega-3 in parenteral nutrition was published by Klek (Klek, 2016).

Table 2 summarizes FDA- and EMA-approved omega-3–based or omega-3-containing emulsion products. All oils, including omega-3 oils, in the formulations are in their natural triacylglyceride forms. These emulsions are stable, partially due to the limited concentrations of EPA and DHA.

2.2.3.4.2. THDG3

THDG3 (DeckTherapeutics, 2024) is an investigational intravenous formulation consisting of a 10% oil-in water emulsion, in which 90% of the oil phase is composed of omega-3 diacylglycerides. The oil phase contains EPA/DHA levels exceeding 85%; however, the diacylglyceride form makes the formulation more stable. The product was initially developed for acute stroke management and is now being advanced for the treatment of hypoxic-ischemic encephalopathy (HIE) (DeckTherapeutics, 2024).

Although intravenous omega-3-based pharmaceutical compositions for treating traumatic brain injury, spinal cord injury, and stroke were previously described in a patent by M. Lewis, those disclosures involve substantially different oil-phase compositions (Lewis, 2017). The drug substance used in THDG3 was originally developed at Ocean Nutrition Canada and DSM (Kralovec et al., 2023), while the diglyceride emulsion format was created in collaboration with Deckelbaum's group at Columbia University (Deckelbaum et al., 2024). THDG3 has demonstrated safety and therapeutic activity in extensive preclinical studies, including rodent models (Zirpoli et al., 2020; Zirpoli et al., 2024) and larger animal models such as piglets and lambs. The program is now prepared to progress into early-phase human clinical trials.

2.2.4. Drugs developed from specialized proresolvin mediators

Specialized pro-resolving mediators (SPMs) are a distinct class of

Table 2. FDA- and EMA-approved omega-3-containing parenteral emulsions

Name	Manufacturer	FDA Approval	EMA Approval	Oil Composition	EPA/DHA Content	Oil Phase (% w/w)
Omegaven®	Fresenius Kabi	2018 (PNAC)	2023 (PNAC)	Fish oil (FO)	EPA 13–26%, DHA 14–27%	10%
SMOFlipid®	Fresenius Kabi	2016 (PN adults); 2022 (PN pediatric)	2004	MCTs, SO, OO, FO	EPA 1.25–2.82%, DHA 0.44–1.04%	20%
Lipidem®/Lipoplus®	B. Braun	Not FDA-approved	2003/2004 (national authorizations)	MCTs, SO, FO	EPA 3.7%, DHA 2.5%	20%
Nutriflex Omega® Omegaflex® Lipoflex®*	B. Braun	Not FDA-approved	2016 (national authorizations)	SO, FO	EPA+DHA 4.4–8.6%	20%

*Administered via peripheral or central venous catheter. FO, fish oil; MCTs, medium-chain triglycerides; OO, olive oil; PNAC, parenteral nutrition-associated cholestasis; SO, soybean oil.

endogenous lipid autacoids biosynthesized from omega-3 and omega-6 polyunsaturated fatty acids, including EPA, DHA, and arachidonic acid (ARA), which actively orchestrate the resolution phase of inflammation rather than simply suppressing pro-inflammatory signalling (Chiang and Serhan, 2020; Fredman and Serhan, 2024). Drug development in this area has focused on overcoming the intrinsic chemical and metabolic instability of native SPMs through the design of metabolically stabilized analogues, receptor-selective agonists, and small-molecule mimetics, as well as through optimized delivery approaches (Fredman and Serhan, 2024; Sousa and Barbosa, 2023). Preclinical studies have demonstrated robust efficacy across a broad range of inflammatory and immune-mediated conditions, including arthritis, inflammatory bowel disease, asthma, cardiovascular disease, neuroinflammation, and pain (Fredman and Serhan, 2024; Chen et al., 2025; Katz et al., 2025). Clinically, progress has been cautious but steady. A limited number of SPM analogs and SPM-pathway modulators have entered early-phase clinical trials (NIH, 2026j; Jannas-Vela et al., 2023; Keeley et al., 2022), primarily for inflammatory, ocular, and pain indications, while no pure SPM-based drug has yet achieved regulatory approval.

2.2.4.1. TP-317

TP-317 (Thetis Pharmaceuticals) is a first-in-class small-molecule investigational drug orally delivering resolvin E1 (RvE1, Figure 1). The preparation is designed to harness the body's own resolving pathways of inflammation. It engages the BLT1 receptor (leukotriene B4 receptor 1) to stimulate tissue repair, promote resolution of inflammation, and restore immune homeostasis without broadly suppressing the immune system. This therapeutic strategy markedly differs from conventional therapies typically employed in chronic inflammatory diseases.

The compound is being advanced in inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis. A Phase Ia first-in-human trial in healthy subjects has been completed, demonstrating a favourable safety, tolerability, and pharmacokinetic profile, with evidence of BLT1 target engagement and predictable systemic exposure (Thetis Pharmaceuticals, 2021, 2024). Phase Ib study in ulcerative colitis patients is planned. TP-317 is being investigated as an adjunct in solid tumour oncology, including colorectal and other cancers (Business Wire, 2026). Its development is backed by wide-ranging patent coverage in major regulatory territories (Thetis Pharmaceuticals, 2021, 2024).

MaR102 TL (Maresins Biopharma, 2026; SPM Therapeutics by Solutex) is the leading maresin-derived therapeutic candidate, originally developed in the C. Serhan laboratory at Harvard University. It is being advanced as a topical formulation for the treatment of localized provoked vulvodynia (LPV). The compound is intended to enhance local resolution of inflammation and pain, reflecting the pro-resolving actions of maresin 1 (Femtech, 2026; Maresins Biopharma, 2026).

Maresins Biopharma has completed preparations for a Phase I/IIa clinical trial evaluating topical MaR102 in women with LPV to assess safety and preliminary efficacy. This early-stage study is expected to characterize the tolerability of the formulation and explore initial signals related to pain reduction and inflammatory endpoints.

2.2.4.2. Navamepent

Navamepent (RX-10045, Figure 1) is a synthetic analog of the endogenous resolvin RvE1 developed as a topical ophthalmic agent to promote resolution of eye inflammation (Gjorstrup and Schwartz, 2010). It reached Phase II clinical evaluation for eye injury but was not advanced further (Torricelli et al., 2014). Like the other investigational drugs mentioned in this section, novamepent aims to mimic pro-resolving actions (counteracting excessive inflammation) rather than simply blocking pro-inflammatory pathways.

2.2.5. Phospholipids

No phospholipid-based drugs are currently approved in North America or Europe. However, products, such as Essentiale® Forte P, and a small number of similar formulations available in other regions, are marketed internationally. Essentiale® Forte P (Opella Healthcare) is an enriched soybean-derived phospholipid preparation offered as a non-prescription product. It is used as nutritional support for liver injury associated with chronic liver disease, cirrhosis, fatty liver, and exposure to hepatotoxic substances. The formulation is supplied in 300-mg capsules (Essentiale, 2026).

2.2.5.1. ETC-588

ETC-588, also known as ESP-24228, first developed by Esperion Therapeutics and later by Pfizer, is an apolipoprotein A1 (APOA1) stimulant (Doggrell, 2004; Drug Bank, 2026b). The therapy consists of large unilamellar vesicles (Figure 1) composed of naturally occurring lipids that circulate through the arterial system, functioning similarly to high-density lipoprotein (HDL) by extracting accumulated cholesterol and other lipids from vessel walls. These

vesicles transport cholesterol from the vasculature to the liver for elimination via the reverse lipid transport pathway, a mechanism proposed to reverse atherosclerosis. Despite this appealing rationale, ETC-588 did not achieve the desired outcomes and was discontinued during Phase II development (Synapse, 2026).

2.2.5.2. Summary

Only a handful of fatty-acid–based medicines have reached the market, and the space is effectively dominated by the omega-3 products Lovaza® and Vascepa®. This narrow success rate highlights how difficult it is to turn lipid biology into reliable therapeutics—issues like formulation instability, variable bioavailability, and inconsistent clinical outcomes have stalled many candidates. The result is a field with broad scientific promise but limited translational payoff, where two well-validated omega-3 drugs overshadow a pipeline that has struggled to deliver comparable efficacy or regulatory-grade evidence.

2.3. Prostaglandins, prostacyclins and their derivatives

Dietary supplements and functional ingredients inspired by prostaglandins and prostacyclins are gaining significant attention for their role in targeting fundamental physiological pathways such as vascular tone, inflammation resolution, and cellular signalling.

There are currently no legal dietary supplements worldwide that contain prostaglandins, prostacyclins, or thromboxanes themselves, due to both scientific constraints and regulatory requirements. However, prostaglandin analogues also demonstrate that lipid-derived or nutrient-related molecules can become major therapeutic classes once purified, standardized, and clinically tested.

Prostaglandins and prostacyclins are bioactive lipid mediators derived from arachidonic acid (ARA) and EPA via the cyclooxygenase (COX) pathway and represent one of the most clinically mature classes of lipid-based therapeutics (Bharata, 2023). Acting through distinct, well-characterized G protein-coupled receptors, these eicosanoids regulate a wide range of physiological processes, including vascular tone, platelet aggregation, inflammation, gastrointestinal protection, renal function, and reproductive biology (Bharata, 2023). Drug development in this area began with the isolation and structural elucidation of native prostaglandins in the mid-20th century and rapidly advanced toward the synthesis of stable, receptor-selective analogues designed to overcome the extreme chemical and metabolic instability of endogenous compounds. This effort yielded multiple approved drugs, including prostaglandin E_1 and E_2 analogues, prostaglandin $F_2\alpha$ analogues widely used in ophthalmology, and prostacyclin (PGI_2) analogues and IP receptor agonists that form the therapeutic backbone of pulmonary arterial hypertension (Abu Deiab and Croatt, 2022; Pluchart et al., 2017). Continuous innovation has produced long-acting formulations, oral and inhaled delivery systems, and non-prostanoid receptor agonists with improved pharmacokinetics and safety profiles. Today, prostaglandin-based and prostacyclin-based drugs are firmly established in clinical practice across cardiovascular, pulmonary, ophthalmic, gastrointestinal, and obstetric indications, with ongoing research focused on next-generation receptor-selective agents, biased agonism, and expanded applications in fibrosis, ischemia-reperfusion injury, and chronic inflammatory diseases (Bharata, 2023; Pluchart et al., 2017; Rondina, 2023).

2.3.1. Prostaglandin E_1

Prostaglandin E_1 (PGE_1, Figure 1) was isolated in crystalline form in 1957 by Bergström and Sjövall (Bergström and Sjövall, 1957) and approved for medical use in the United States in 1981 (Sneader, 2005). Together with its derivatives, they have been used to treat various medical conditions. Prostaglandin E_1 is a vasodilator, and its various effects in the body include opening blood vessels, relaxing smooth muscle, inhibiting clotting, and causing uterine contractions (Kirtland, 1988).

Alprostadil is a PGE_1 created by total synthesis. It was first produced by the Upjohn Company in the early 1970s (Drugs 2026c). In infants with certain congenital heart defects, alprostadil is delivered by slow injection into a vein to maintain a patent *ductus arteriosus* until surgery can be carried out (Ainsworth, 2020). Alprostadil is also used to treat erectile dysfunction (Hanchanale and Eardley, 2014).

2.3.2. Misoprostol

Misoprostol and lubiprostone (Figure 1) are synthetic derivatives of PGE_1. Misoprostol decreases gastric acid secretion and protects the gastric mucosa from injury associated with aspirin and other nonsteroidal anti-inflammatory drugs (Drugs, 2026d). It also has several established obstetric applications, including the induction of abortion or labour and the prevention and treatment of postpartum hemorrhage (Ainsworth, 2020; Padayachee et al., 2020). In cases where other therapies are ineffective, misoprostol may be used to treat duodenal ulcers and manage peptic ulcer disease (Dudzinski and Seerhan, 2017; Ballinger,1994). The drug is included on the WHO Model List of Essential Medicines for its obstetric uses (WHO, 2026b).

2.3.3. Lubiprostone

Lubiprostone (Amitiza®; Mallinckrodt, Takeda) is a PGE_1 derivative indicated for the treatment of chronic constipation (Lacy, 2006). Originally discovered by Sucampo Pharmaceuticals, it received US FDA approval in 2006 (US FDA, 2026e). The FDA subsequently expanded its indications in 2008 to include irritable bowel syndrome with constipation (Lang, 2008) and in 2013 for opioid-induced constipation in adults with chronic non-cancer pain (Webster et al., 2018). Health Canada approved it in 2015 (Health Canada, 2015).

2.3.4. Bimatoprost

Bimatoprost (Figure 1, Lumigan®, Latisse®) is a prostaglandin $F_2\alpha$ analogue first described in a patent issued to Allergan Inc. (Woodward et al., 1994). It is prescribed to lower elevated intraocular pressure, including in glaucoma, and is particularly used for open-angle glaucoma when other therapies are insufficient (Drugs, 2026e; Patil et al., 2009). Its therapeutic action stems from enhancing the outflow of aqueous humour from the eye. Bimatoprost was also later found to promote hair growth, leading to its use in treating eyelash, eyebrow, and scalp alopecia and its approval for increasing eyelash length (DailyMed, 2026; Barrón-Hernández and Tosti, 2017). The drug received its first US FDA approval in 2001, and more than one million prescriptions are written annually in the United States (ClinCalc, 2026).

2.3.5. Latanaprost

Latanoprost (Figure 1, Xalatan®; originally developed by Pharmacia, later Pharmacia & Upjohn) is a prostaglandin $F_2\alpha$ analogue structurally related to bimatoprost, differing by the substitution

Table 3. FDA- and EMA-approved prostaglandin-based medicines

Name	Brand/Other Names	Manufacturer	FDA Approval	EMA Approval	Composition/Class
Alprostadil (PGE_1)	Prostin VR® (CHD), Caverject® (ED), Muse® (ED), Vitaros® (ED)	Upjohn, Pfizer, Vivus	1981 (CHD); 1995–1996 (ED)	2013 (ED)	PGE_1
Misoprostol	Cytotec®, Hemoprostol®	G.D. Searle/Pfizer	1988 (NSAID-ulcer prevention)	2014 (PPH; national authorizations for MA, IL)	PGE_1 derivative
Lubiprostone	Amitiza®	Sucampo, Mallinckrodt, Takeda	2006 (CIC); 2008 (IBS-C); 2013 (OIC)	No centralized approval; recommended for national authorization since 2015	PGE_1 derivative
Bimatoprost	Lumigan®, Latisse®, Durysta®, Zolymbus®	Allergan (AbbVie)	2001 (EIOP); 2008 (H); 2020 (G)	2002, 2010 (EIOP)	$PGF_2\alpha$ analogue
Latanoprost	Xalatan®, Lyuzeh®*	Pharmacia/Pharmacia-Upjohn	1996 (EIOP)	1996 (EIOP); 2022 (EIOP)	$PGF_2\alpha$ analogue
Epoprostenol (PGI_2)	Flolan®, Veletri®**	GSK; J&J/Actelion	1995 (PPHT); 2010	2013 (decentralized, PPHT)	PGI_2
Iloprost	Ventavis®***, Aurlumyn®****, Ilomedin®*****	Bayer Schering; Essential Pharma; Actelion	2004 (PAH); 2024 (FB)	2003 (PAH)	PGI_2 analogue
Treprostinil	Remodulin®******, Orenitram® (oral), Tyvaso®***, Yutrepia®, Trepulmix®	United Therapeutics	2002 (PAH); 2023; 2009/2022 (PAH); 2021 (PH-ILD); 2025	2020 (CTPH)	PGI_2 analogue

*Preservative-free formulation. **More stable formulation. ***Inhalation. ****Injection. *****Intravenous. ******Infusion. CHD, congenital heart defects; CIC, chronic idiopathic constipation; CTPH, chronic thromboembolic pulmonary hypertension; ED, erectile dysfunction; EIOP, elevated intraocular pressure; FB, frostbite; G, glaucoma; H, hypotrichosis; IBS-C, irritable bowel syndrome. constipation; IL, induced labour; MA, medical abortion; NSAID, non-steroidal anti-inflammatory drug; OIC, opioid-induced constipation; PAH, pulmonary arterial hypertension; PPH, postpartum hemorrhage; PPHT, primary pulmonary hypertension; PH-ILD, pulmonary hypertension associated with interstitial lung disease.

of the carboxyl group with an isopropyl ester rather than an ethyl amide (Resul et al.,1993). It is used to lower elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension (Stjernschantz and Alm,1996). It was the first prostaglandin analog approved for this purpose. Administered as an ophthalmic solution (Drugs, 2026f), it increases aqueous humour outflow through the uveoscleral pathway (Patel and Spencer, 1996).

Latanoprost functions as a selective agonist of the prostaglandin F receptor and undergoes hepatic metabolism via fatty-acid β-oxidation to 1,2-dinor- and 1,2,3,4-tetranor-latanoprost acid. It received regulatory approval from both the US FDA and the EMA in 1996 (Drugs, 2026f; EMA, 2026c) and is included in the World Health Organization's List of Essential Medicines (WHO, 2026c).

2.3.6. Prostacyclin

Epoprostenol is the pharmaceutical form of prostacyclin (prostaglandin I_2, PGI_2, Figure 1), a potent inhibitor of platelet activation and a strong vasodilator. Prostacyclin was discovered in 1976, initially referred to as "prostaglandin X" (Moncada et al., 1976) and its chemical synthesis was reported the following year (Johnson et al., 1977). Clinically, epoprostenol is used in the management of pulmonary arterial hypertension (Ruopp and Cockrill, 2022; Drugs, 2026g) and has also been applied in conditions such as pulmonary fibrosis and atherosclerosis (Stitham et al., 2011).

2.3.7. Iloprost

Iloprost (Figure 1, Ventavis®, Aurlumyn®) is a synthetic analogue of prostacyclin. Originally developed by Schering AG, it is currently marketed by Bayer in the EU and by Actelion Pharmaceuticals in the United States. The drug can be administered intravenously, subcutaneously, or via inhalation (Bayer, 2026). Iloprost is indicated for pulmonary arterial hypertension (PAH), scleroderma, Raynaud's phenomenon, frostbite, and other conditions characterized by severe vasoconstriction and impaired tissue perfusion (EMA, 2026d). The EMA approved iloprost (Ventavis®) in 2003, followed by US FDA approval in 2004 (Drugs, 2026h). In 2024, iloprost (Aurlumyn®) also received US approval specifically for the treatment of frostbite (Harris, 2024).

2.3.8. Treprostinil

Treprostinil (Figure 1) is a tricyclic analogue of prostacyclin 3 marketed under several formulations: Remodulin® for infusion, Orenitram® for oral administration, and Tyvaso® for inhalation. It functions as a vasodilator to treat symptoms of pulmonary arterial hypertension (PAH) (Torres and Rubin, 2013). Treprostinil is indicated for patients with PAH who develop New York Heart Association (NYHA) Class II–IV symptoms, and emerging evidence suggests potential benefit in Degos disease as well (Shapiro et al., 2013). The drug received EU approval in 2020 (EMA, 2026e) while the US FDA has authorized multiple formulations across seven approvals issued between 2002 and 2025 (PHA, 2026).

2.3.9. Summary

Table 3 offers a consolidated summary of the indications for all

Table 4. FDA- and EMA-approved retinoid-based medicines

Name (Generic)	Brand/Other Names	Manufacturer	FDA Approval	EMA Approval	Composition/Class
Tretinoin	Retin-A®, Altreno®, Twyneo®, Vesanoid®**	UPenn; Ortho; J&J; Bausch	1971 (AV); 1995 (PA); 1998* (PA); 2018 (AV); 2021 (AV); 1995 (APL)	2016–2018 regulatory review	(7E,9E,11E,13E)-retinoic acid
Isotretinoin	Accutane®, Roaccutane®	Hoffmann-La Roche; Upsher-Smith; Amneal	1982 (SRA)	Authorized 1983	(7E,9E,11E,13Z)-retinoic acid
Acitretin	Soriatane®, Neotigason®	Hoffmann-La Roche; Stiefel/GSK	1996 (RP/PDC)	1984 (RP/PDC)	Aromatic retinoid

*Tretinoin cream generic. **oral formulation. APL, acute promyelocytic leukemia; AV, acne vulgaris; PA, photoaging; RP/PDC, resistant psoriasis/pustular dermatological conditions; SRA, severe recalcitrant acne.

FDA-approved and EMA-approved prostaglandin-based medicines examined in this review. Prostaglandin-based drugs—ranging from classic agents like alprostadil and misoprostol to modern prostacyclin analogues and glaucoma therapies—showcase both the versatility and the limitations of this pathway. Their success stems from potent, well-defined physiologic actions, yet that same potency brings drawbacks: short half-lives, delivery challenges, and frequent adverse effects that restrict broader use. While epoprostenol and its analogues transformed pulmonary hypertension care, and prostaglandin analogues revolutionized glaucoma treatment, the overall field remains fragmented, with each agent thriving only in narrow therapeutic niches rather than achieving broad pharmacologic dominance.

2.4. Retinoids (vitamin A derivatives)

Retinoid-based dietary supplements have grown in popularity because vitamin A and its derivatives play indispensable roles in vision, immune resilience, epithelial integrity, and healthy skin. Modern diets often fall short in providing consistent amounts of bioavailable retinoids, and consumers increasingly turn to supplements to support eye health, immune function, and overall cellular renewal. Their importance is reinforced by strong clinical evidence linking vitamin A status to night vision, mucosal defence, and normal developmental processes. Popular examples include retinyl palmitate, retinyl acetate, lutein, zeaxanthin and beta-carotene, as well as mixed carotenoid blends from algae, carrots, and palm fruit. These ingredients are widely used in multivitamins, skin-health formulations, and targeted eye-health supplements, reflecting the enduring demand for safe, well-studied retinoid nutrition.

Retinoids and vitamin A derivatives constitute a well-established class of lipid-derived signalling molecules that regulate cell differentiation, proliferation, apoptosis, and immune function primarily through activation of nuclear retinoic acid receptors (RARs) and retinoid X receptors (RXRs), which act as ligand-activated transcription factors (Le Maire et al., 2012). Drug development has focused on synthesizing structurally modified retinoids with improved receptor selectivity, metabolic stability, and reduced toxicity, leading to several clinically important agents (Kawczak et al., 2024), and highly targeted retinoid therapies exemplified by all-trans-retinoic acid in acute promyelocytic leukemia, where it induces terminal differentiation of malignant cells (Le Maire et al., 2012). Retinoid-based drugs are currently approved and widely used in dermatology, oncology, and ophthalmology, while ongoing development explores selective RAR/RXR modulators, topical and tissue-targeted formulations, and combination regimens to expand efficacy while mitigating class-limiting adverse effects such as teratogenicity and mucocutaneous toxicity (Xu et al., 2024).

2.4.1. Tretinoin

Retinoic acid (all-trans-retinoic acid) is a biologically active metabolite of retinol (vitamin A_1) essential for embryonic development, male fertility, bone growth regulation, and immune function. In its pharmaceutical form, it is known as tretinoin (Retin-A®, Johnson & Johnson), with numerous manufacturers producing the active ingredient. Tretinoin (Figure 1) is used clinically to treat acne and acute promyelocytic leukemia (Yoham and Casadesus, 2023). For acne, it is administered topically as a cream, gel, or ointment (Baldwin et al., 2021), and it remains the most extensively studied retinoid for photoaging (Siddiqui et al., 2024).

Because tretinoin is available in multiple formulations, it holds several FDA approvals, with the first granted in 1998 (Drugs, 2026i). It is also included on the World Health Organization's List of Essential Medicines (WHO, 2026b).

2.4.2. Isotretinoin

Isotretinoin (Figure 1) is a geometric isomer of tretinoin and occurs naturally in the body at low levels. Best known under the brand name Accutane®, among many others, it is an oral therapy primarily prescribed for severe, treatment-refractory acne (Burton et al., 1984; Mohiuddin, 2019; Shingari et al., 2025). Isotretinoin has also been used off label for basal cell and squamous cell carcinomas; however, it does not hold any formal approval for these indications due to a lack of clinical evidence demonstrating efficacy (Clouser et al., 2010).

2.4.3. Acitretin

Acitretin (Figure 1), marketed under the brand names Neotigason® and Soriatane®, is a second-generation oral retinoid primarily used in the management of psoriasis (Zito and Mazzoni, 2021; Guenther et al., 2017). It received the US FDA approval in 1996 (Ghasri et al., 2011).

Because of its potency and systemic activity, acitretin is generally reserved for severe, treatment-refractory psoriasis. Its mechanism involves binding to nuclear retinoic acid receptors, thereby modulating gene transcription, promoting keratinocyte differentiation, and suppressing epidermal hyperplasia. These combined actions reduce the excessive cellular proliferation that characterizes psoriatic plaques.

Third-generation retinoids such as bexarotene and adapalene—engineered with rigid, polyaromatic scaffolds that selectively target specific retinoic acid receptor subtypes (primarily RAR-β and RAR-γ)—are not discussed here because they lack

structural similarity to tretinoin, isotretinoin or acitretin, including the characteristic tetraene (polyene) side chain. Table 4 lists all FDA- and EMA-approved retinoid-based therapeutics listed in this review.

2.4.4. Summary

Retinoids like tretinoin, isotretinoin, and acitretin remain some of the most powerful dermatologic drugs, but their success is tempered by well-known limitations. Their efficacy in acne, photoaging, and keratinization disorders is unmatched, yet they carry a narrow therapeutic window marked by irritation, teratogenicity, and systemic toxicity at higher exposures. Long-term adherence is often poor because visible benefits arrive slowly while side effects appear quickly. And although they influence fundamental pathways of skin biology, their utility remains confined to specific indications rather than broad dermatologic transformation.

3. Synthesis, cross-class insights, and future directions for lipid-based therapeutics

Lipids and lipid-derived pharmaceuticals occupy a distinctive but unevenly developed position within the global drug landscape. Although they represented only a modest share of the USD 1.8 trillion global pharmaceutical market in 2025, their clinical and commercial impact is disproportionately large in several therapeutic areas. North America —comprising the United States, Canada, and Mexico—accounts for more than half of global pharmaceutical sales (BioSpace, 2026), creating a favourable environment for lipid-based drugs with strong regulatory and reimbursement support.

The preceding sections outlined the major therapeutic classes—fatty acids and their derivatives, prostaglandins, and retinoids—successful drugs alongside numerous investigational agents that failed to progress. This final section integrates these observations to identify the mechanistic, clinical, and commercial determinants that consistently shape success or failure across lipid-based drug categories.

3.1. Convergent features of successful lipid-based drugs

3.1.1. Clear, dominant mechanisms of action

Despite their chemical diversity, successful lipid-based drugs share a well-defined primary mechanism with predictable downstream effects. For instance:

- Icosapent ethyl (EPA) lowers triglycerides and shifts eicosanoid production toward less inflammatory species (Borghi and Bragagni, 2023).
- Bempedoic acid inhibits ATP-citrate lyase, producing a clean metabolic effect without the pleiotropy of PPAR dual agonists (Paton, 2017).
- Prostaglandin analogues (latanoprost, bimatoprost) engage specific GPCRs with highly localized actions (Zhou et al., 2022).
- Retinoids activate nuclear retinoic acid receptors with unusually clear structure–activity relationships (Kawczak et al., 2024).

This mechanistic clarity facilitates dose selection, biomarker development, and regulatory acceptance - factors often missing in slowly progressing or failed investigational compounds such as ibrilatazar, OMT-28, CXA-10, and AVX-001.

3.1.2. Controllable pharmacokinetics and localized delivery

Lipid molecules are inherently prone to broad distribution and metabolic promiscuity. Successful drugs constrain these tendencies through short half-lives, targeted delivery, or stable formulations.

- Ophthalmic prostaglandins achieve potent intraocular pressure reduction with minimal systemic exposure (Sridharan, 2024).
- Parenteral prostacyclins (epoprostenol, treprostinil, iloprost) use controlled infusion or inhalation to manage systemic vasodilation (Gomberg-Maitland and Olschewski, 2008).
- Topical retinoids deliver high local concentrations while limiting systemic toxicity (Shroot, 1986).
- Ethyl-ester omega-3 formulations (Vascepa®, Lovaza®) improve stability and dosing precision compared with free-fatty-acid preparations. (US FDA, 2026f).

3.1.3. Strong, clinically meaningful endpoints

Outcome-level evidence has been central to the adoption of lipid-based drugs:

- REDUCE-IT demonstrated cardiovascular event reduction for icosapent ethyl (Harris, 2019).
- CLEAR Outcomes confirmed cardiovascular benefit for bempedoic acid (Nichols et al., 2024).
- Prostacyclin therapies consistently improve survival and functional capacity in (Barnes et al., 2019).
- Retinoids provide visible, quantifiable dermatologic improvements (Weiss et al., 1988).
- These endpoints align with guideline-driven markets where regulatory and reimbursement frameworks reward demonstrable clinical benefit.

3.1.4. Manageable safety profiles

Even when toxicity exists, successful agents offer a favorable benefit-risk balance within their therapeutic context.

- Retinoids carry teratogenic (Heckel et al., 1993) and mucocutaneous (Uzuncakmak and Karadag, 2019) risks but remain indispensable in dermatology.
- Valproate's risks are offset by its efficacy in epilepsy and bipolar disorder.
- Local delivery of prostaglandins and prostacyclins mitigates systemic adverse effects.

3.2. Market performance across lipid-based drug classes

3.2.1. Omega-3 fatty acids and PUFA-derived drugs

The global prescription omega-3 market was valued at USD 1.4 billion in 2024 and is projected to reach USD 3.0 billion by 2034 (MarketUS, 2026). Growth is driven by:

- Rates of cardiovascular disease and obesity.
- Strong physician confidence in omega-3 therapies.
- Broad reimbursement in North America (GrandView Research, 2026; Mordor Intelligence, 2026).
- Expanding access in China.

Despite this, only two major products—Vascepa® and Lovaza®—remain on the market, as multiple follow-on candidates (Epanova®, Lypdiso™, icosabutate, OMT-28) failed to demon-

Table 5. Mechanism, indication, regulatory status, and translational outcome of all examined lipid-based therapeutics in this review

Drug/Compound	Mechanism	Indication	Regulatory Status	Translational Outcome
SECTION A—Fatty acids and fatty-acid derivatives				
Sodium butyrate	HDAC inhibition; SCFA signalling	Inflammation, metabolic disorders, and neurology	ODD in the EU	Preclinical/ early clinical
Valproate	HDAC inhibition; fatty-acid mimic	Epilepsy, bipolar disorder	FDA/EMA approved	Successful repurposed therapy
Triheptanoin	Anaplerotic odd-chain triglyceride	LC-FAOD, epilepsy	FDA 2020	Approved metabolic therapy
Etomoxir	CPT-1 inhibition; PPARα agonist	Heart failure, metabolic modulation, neuro-oncology	Not approved	Discontinued (toxicity)
Bempedoic acid	ACLY inhibition	Hypercholesterolemia	FDA/EMA approved	Marketed a cardiovascular drug
Lorenzo's Oil	VLCFA synthesis inhibition	X-ALD	Not approved	Medical food: limited efficacy
LAM561	Membrane lipid therapy	Cancer, glioblastoma	Investigational	Discontinued
Ibrilatazar	Dual PPAR-α/γ agonist	Cancer	Phase III, ODD designation	Discontinued
OMT-28	AMPK/Sirt1/PGC1-a network activation	Mitochondrial dysfunction, inflammation	Investigational	Early development
CXA-10	Nitro-fatty acid; Nrf2 activation	PAH, kidney disease	Phase II	Ongoing development
Icosapent ethyl	Reducing hepatic VLDL-TG synthesis; increased β−oxidation	HTG, CVD risk	FDA 2013; expanded 2019	Successful; widely marketed
Lovaza®/Omacor®	Decreased lipogenesis; increased β−oxidation	HTG	FDA 2004; EMA 1999	Marketed; multiple generics
Epanova®	Decreased lipogenesis; increased β−oxidation	Severe HTG	FDA 2014	Discontinued
Alfa (EPAspire™)	Rapid absorption; IMM; membrane integration	FAP, ARDS	Investigational	Discontinued
Lypdiso™	Decreased lipogenesis; increased β-oxidation	HTG	FDA-approved generic	Marketed
Edasalonexent	NF-κB inhibition	DMD	Phase III failed	Discontinued
LAM226	Reducing tau hyperphosphorylation; restoration of SNAP-25	Neurodegenerative diseases, Alzheimer's	Investigational	Early development
Icosabutate	FFAR1and FFAR4 activation; anti-inflammatory; antifibrotic	MASH	Phase II	Ongoing development
AVX-001	$cPLA_2$ inhibitor	Psoriasis	Phase II	Discontinued
Omegaven®	Reducing inflammation; boosting β-oxidation	PNAC	FDA 2018; EMA 2023	Approved parenteral therapy
THDG3	Pleiotropic effects	HIE, stroke management	Preclinical	Preclinical
TP-317	ω-3 derivative	IBD, cancer	Investigational	Early development
MaR102 TL	Inflammation resolution	LPV	Preclinical	Early research
Navamepent (RX-10045)	Inflammation resolution Pro-resolving actions mimicking	Dry eye	Phase II	Development uncertain
ETC-588	Accumulated cholesterol extraction; atherosclerosis reversal	Cardiovascular inflammation	Phase II	Development paused
SECTION B—Prostaglandins, prostacyclins, and derivatives				
Alprostadil (PGE_1)	Vasodilator; binding to PGE_1 receptors; increases cAMP	CHD, ED	FDA 1981–1996; EMA 2013	Widely used

(continued)

Table 5. *(continued)*

Drug/Compound	Mechanism	Indication	Regulatory Status	Translational Outcome
Misoprostol	Gastric acid secretion reduction; binding to specific PG receptors	NSAID-ulcer prevention, PPH, MA, OA	FDA 1988; EMA national	Global standard therapy
Lubiprostone	CIC-2 channel activation	CIC, IBS-C, OIC	FDA 2006–2013	Marketed
Bimatoprost	Mimicking naturally occurring prostamides	G, H	FDA 2001–2020; EMA 2002–2010	Widely used
Latanoprost	PGF receptor agonist	G, OH	FDA 1996; EMA 1996/2022	First-line therapy
Epoprostenol (PGI_2)	Vasodilator, binds to PGI receptor, increases cAMP	PAH, PF	FDA 1995; EMA 2013	Lifesaving PAH therapy
Iloprost	Vasodilator, binds to prostanoid receptors, increases cAMP	PAH, frostbite	FDA 2004/2024; EMA 2003	Approved inhaled/IV therapy
Treprostinil	Vasodilator; anti-platelet aggregation; prostanoid receptors affinity	PAH, PH-ILD, CTPH	FDA 2002–2025; EMA 2020	Major PAH drug
SECTION C—Retinoids				
Tretinoin	RAR & RXR agonist; collagen production stimulation	Acne, APL, PA	FDA 1971–2021; EMA review	Successful dermatologic/oncologic therapy
Isotretinoin	RAR agonist; induction of FoxO proteins	Severe acne	FDA 1982; EMA 1983	Highly effective; widely used
Acitretin	Retinoid (RAR/RXR modulation)	Psoriasis, PDC	FDA 1996; EMA 1984	Standard systemic retinoid

ACLY, ATP-citrate lyase; ARDS, acute respiratory distress syndrome; APL, acute promyelocytic leukemia; cAMP, cyclic adenosyl monophosphate; CHD, congenital heart defects; CIC, chronic idiopathic constipation; CPT-1, carnitine palmitoyl transferase 1; CVD, cardiovascular disease; $cPLA_2$, cytosolic phospholipase A_2; DMD, Duchenne muscular dystrophy; ED, erectile dysfunction; FAP, familial adenomatous polyposis; G, glaucoma; H, hypotrichosis; HDAC, histone deacetylase; HIE, hypoxic ischemic encephalopathy; HTG, high triacyl glycerides; IBD, irritable bowel disease; IBS-C, irritable bowel syndrome constipation; IMM, inflammatory mediators modulation; LC-FAODs, long-chain fatty oxidation disorder; LPV, localized provoked vulvodynia; MA, medical abortion; MASH, metabolic dysfunction-associated steatohepatitis; NF-κB, nuclear factor κB; Nrf2, nuclear factor erythroid 2-related factor 2; OA, obstetric applications; ODD, orphan drug designation; OIC, opioid-induced constipation; PA, photoaging; PAH, pulmonary arterial hypertension; PDC, pustular dermatological conditions; PH, pulmonary fibrosis; PH-ILD, pulmonary hypertension associated with interstitial lung disease; PNAC, parenteral nutrition-associated cholestasis; PPAR, peroxisome proliferator-activated receptors; PPH, postpartum hemorrhage; RAR, retinoic acid recepror; RXR, retinoid X receptor; SCFA, short-chain fatty acid; SNAP-25, synaptosome associated protein of 25 KDa; VLCFA, very long-chain fatty acid; VLDL-TGs, very low density lipoprotein triacyl glycerides; X-ALD, X-linked adrenoleukodystrophy.

strate outcome-level benefit or acceptable tolerability.

A key emerging trend in the global omega-3 prescription market is the European Commission's approval of plant-based omega-3 products (Nichols, 2022).

SPM-based therapeutics remain scientifically promising but commercially immature due to chemical instability and manufacturing challenges (Maliha et al., 2024).

3.2.2. Prostaglandins and prostacyclins

Prostaglandin-based therapeutics span two major markets:

- Ophthalmic prostaglandin analogues (latanoprost, bimatoprost):
  - Market size: USD 3.54 billion in 2024;
  - Projected: USD 6.38 billion by 2034 (Precedence Research, 2026a);
  - North America accounts for 40–45% of global revenues (Precedence Research, 2026a, Tripathy, Patel, and Geetha, 2024).
- Systemic prostaglandins (misoprostol, alprostadil):
  - Market size: USD 0.5–0.6 billion in 2024–2025;
  - Projected: >USD 1.16 billion by 2035 (GlobalGrowth, 2026).

Prostacyclin analogues and IP-receptor agonists (epoprostenol, treprostinil, iloprost) are typically reported within PAH portfolios rather than as a standalone lipid-mediator market.

3.2.3. Retinoids

Retinoids benefit from the high global prevalence of acne and other dermatologic conditions.

- Market size: USD 0.84 billion in 2025 (Precedence Research, 2026b).
- Projected: USD 1.62 billion by 2035.
- When OTC and combination products are included, the retinoid segment exceeded USD 3.3 billion in 2022 (GlobeNewswire, 2026a).

Their long clinical history and clear nuclear-receptor pharmacology have made retinoids one of the most commercially successful lipid-derived drug classes.

3.3. Recurrent causes of failure in lipid-based drug development

3.3.1. Mechanistic ambiguity

Agents such as ibrilatazar, icosabutate, OMT-28, CXA-10, and AVX-001 targeted broad inflammatory or metabolic pathways without a dominant clinical effect, complicating dose selection and endpoint justification.

3.3.2. Safety liabilities

Examples include:
- Etomoxir: hepatotoxicity from irreversible CPT-1 inhibition (Holubarsch et al., 2007).
- PPAR-α/γ dual agonists: edema, weight gain, cardiovascular concerns (Nissen et al., 2005).
- Edasalonexent: insufficient efficacy at tolerable doses (Finkel et al., 2021).

3.3.3. Chemical instability and formulation barriers

- SPMs and nitro-fatty acids degrade rapidly.
- Free-fatty-acid omega-3 formulations (Epanova®, Lypdiso™) produced poor outcomes and GI intolerance (Nichols et al., 2020; NIH, 2026h; Maki et al., 2022).

3.3.4. Market and regulatory misalignment

Some candidates targeted small or poorly defined markets or competed with entrenched generics, limiting commercial viability.

3.4. Cross-class comparison

- Fatty acids succeed when mechanisms are clean and metabolic (EPA, bempedoic acid) and fail when pleiotropy or toxicity dominates (etomoxir, PPAR dual agonists).
- Prostaglandins succeed due to potent, short-acting, locally deliverable pharmacology aligned with clear physiological roles; failures arise when systemic exposure becomes unmanageable.
- Retinoids succeed through precise nuclear-receptor targeting and topical delivery; systemic retinoid use is limited by toxicity.

Across all classes, the unifying principle is that lipids become successful therapeutics only when their inherent biological promiscuity is constrained by formulation, delivery, and a sharply defined clinical purpose.

3.5. Future directions

Promising areas for future development include:
- Intravenous omega-3 emulsions as neuroprotectants in hypoxic-ischemic injury (Zirpoli et al., 2024).
- Stable SPM analogues capable of modulating inflammation-resolution pathways (Byrne and Guiry, 2024).
- Next-generation retinoids with improved receptor selectivity (Luczak et al., 2025).
- Novel metabolic lipid modulators for cardiovascular and metabolic diseases (Brandts and Ray, 2023).

The field is moving toward precision lipid pharmacology, in which endogenous lipid pathways are modulated with greater specificity, stability, and clinical relevance (Touyz, 2024).

Table 5 presents a comparative overview of all drugs discussed in this review, summarizing their mechanisms, indications, regulatory status, and translational outcomes.

3.6. Concluding perspective

Lipid-based therapeutics have progressed from biochemical curiosities to indispensable drugs, yet their trajectory reveals a striking imbalance: a handful of successes—EPA ethyl esters, prostaglandin analogues, prostacyclins, retinoids—dominate clinical practice while most lipid-derived candidates fail to translate. This contrast is even sharper when viewed through the food-as-medicine lens: although many bioactive lipids originate in foods, only a few—such as EPA and DHA from fish oil or butyrate derivatives from dairy fats—have successfully made the leap from dietary components to regulated pharmaceuticals or medical foods. Their success underscores a central principle: lipids can become safe, effective, commercially viable medicines when their mechanisms are precisely defined and their delivery tightly controlled, but they falter when stability, specificity, or clinical endpoints are misaligned. Across omega-3 agents, parenteral emulsions, prostaglandins, and retinoids, the same lesson recurs—potent biology alone is not enough. As lipid chemistry, structural biology, and formulation science advance, future breakthroughs will likely emerge from highly targeted interventions that harness endogenous lipid signaling while capturing the therapeutic potential long hinted at in food-derived bioactives.

References

Abu Deiab, G.I., and Croatt, M.P. (2022). Prostacyclin (PGI_2) scaffolds in medicinal chemistry: Current and emerging drugs. Med. Chem. Res. 31: 1241–1251.

Adebesin, A.M., Wesser, T., Vijaykumar, J., Konkel, A., Paudyal, M.P., Lossie, J., Zhu, C., Westphal, C., Puli, N., Fischer, R., Schunck, W.H., and Falck, JR (2019). Development of robust 17(*R*),18(*S*)-epoxyeicosatetraenoic acid (17,18-EEQ) analogues as potential clinical antiarrhythmic agents. J. Med. Chem. 62(22): 10124–10143.

Adam, W., Lazarus, M., Schmerder, A., Humpf, H.-U., Saha-Möller, C.R., and Schreier, P. (1998). Synthesis of optically active α-hydroxy acids by kinetic resolution through lipase-catalyzed enantioselective acetylation. Eur. J. Org. Chem. 1998(9): 2013–2018.

Ainsworth, S. (2020). Drug Use in Pregnancy and the First Year of Life. Neonatal Formulary. (8th ed.). Oxford Academic, Oxford, pp. 525–527.

Alberts, B. (2015). Molecular Biology of the Cell. (6th ed.). W.W. Norton & Company, New York, pp. 72-90 and 615-690.

Amschler, H., Eistetter, K., Ludvig, G., Rapp, E., and Wolf, H. (1983). Substituted oxirane carboxylic acids, process for their preparation, their use and medicines containing them. EP0025192.

Avila, A., Málaga, I., Sirsi, D., Kayani, S., Primeaux, S., Kathote, G.A., Jakkamsetti, V., Kallem, R.R., Putnam, W.C., Park, J.Y., Shinnar, S., and Pascual, J.M. (2023). Combination of triheptanoin with the ketogenic diet in glucose transporter type 1 deficiency (G1D). Sci. Rep. 13(1): 8951.

Baldwin, H., Webster, G., Stein Gold, L., Callender, V., Cook-Bolden, F.E., and Guenin, E. (2021). Fifty years of topical retinoids for acne: Evolution of treatment. Am. J. Clin. Dermatol. 22(3): 315–327.

Ballantyne, C.M., Bays, H.E., Kastelein, J.J., Stein, E., Isaacsohn, J.L., Braeckman, R.A., and Soni, P.N. (2012). Efficacy and safety of eicosapentaenoic acid ethyl ester (AMR101) therapy in statin-treated patients with persistent high triglycerides (from the ANCHOR Study). Am. J. Cardiol. 110(7): 984–992.

Ballinger, A. (1994). Cytoprotection with misoprostol: Use in the treatment and prevention of ulcers. Dig. Dis. 12(1): 37–45.

Barnes, H., Yeoh, H-L., Fothergill, T., Burns, A., Humbert, M., and Williams, T. (2019). Prostacyclin for pulmonary arterial hypertension. Cochrane Database of Systematic Reviews (5): CD012785.

Barrón-Hernández, Y.L., and Tosti, A. (2017). Bimatoprost for the treatment of eyelash, eyebrow and scalp alopecia. Expert Opin. Investig. Drugs 26(4): 515–522.

Bayer, AG (2026). Ventavis INN Iloprost: Summary of product characteristics. https://www.bayer.com/sites/default/files/ventavis-smpc-dec-2021-0.pdf. Accessed 4 Feb. 2026.

Bays, H.E., Ballantyne, C.M., Kastelein, J.J., Isaacsohn, J.L., Braeckman, R.A., and Soni, P.N. (2011). Eicosapentaenoic acid ethyl ester (AMR101) therapy in patients with very high triglyceride levels (from

the multi-center, placebo-controlled, randomized, double-blind, 12-week study with an open-label extension [MARINE] Trial). Am. J. Cardiol. 108(5): 682–690.
Berg, J., Gatto, G. Jr, Hines, J., Tymoczko, J.L., and Stryer, L. (2023). Biochemistry. (10th ed.). MacMillan Learning, New York, pp. 341–363.
Bergstrom, S., and Sjövall, J. (1957). Isolation of Prostaglandin. Acta Chim. Scand. 11: 1086.
Berlin, S., Goette, A., Summo, L., Lossie, J., Gebauer, A., Al-Saady, N., Calo, L., Naccarelli, G., Schunck, W.H., Fischer, R., Camm, A.J., and Dobrev, D. (2020). Assessment of OMT-28, a synthetic analog of omega-3 epoxyeicosanoids, in patients with persistent atrial fibrillation: Rationale and design of the PROMISE-AF phase II study. Int. J. Cardiol. Heart Vasc. 129: 100573.
Bharata, A. (2023). Pharmacology of prostaglandin analogues. Pharmacology Mentor. https://pharmacologymentor.com/pharmacology-of-prostaglandin-analogues. Accessed 4 Feb. 2026.
Bhatt, D.L., Steg, P.G., Miller, M., Brinton, E.A., Jacobson, T.A., Ketchum, S.B., Juliano, R.A., Jiao, L., Doyle, R.T. Jr, and REDUCE-IT investigators. (2019). Cardiovascular risk reduction with icosapent ethyl for hypertriglyceridemia. Circulation 380(1): 11–22.
BioSpace. (2026). Pharmaceutical market size report. https://www.biospace.com/press-releases/pharmaceutical-market-size-to-surpass-usd-2-82-trillion-by-2033. Accessed 4 Feb. 2026.
Borghi, C., and Bragagni, A. (2023). Clinical results and mechanism of action of icosapent ethyl. Eur. Heart J. 25(Suppl B): B37–B40.
Bosch-Barrera, J., Estévez-García, P., Martín-Martorell, P., Sabatier, R., Nadal, E., Sais, E., Gascón, P., Oaknin, A., Rodon, J., Lizcano, J.M., Muñoz-Guardiola, P., Fierro-Durán, G., Pedrós-Gámez, O., Pérez-Montoyo, H., Yeste-Velasco, M., Cortal, M., Pérez-Campos, A., Alfón, J., Domènech, C., and Morán, T. (2025). ENDOLUNG trial part II. Lung Cancer 201: 108105.
Brandts, J., and Ray, K.K. (2023). Novel and future lipid-modulating therapies for the prevention of cardiovascular disease. Nat. Rev. Cardiol. 20(9): 600–616.
Burton, C.S., Eyre, R.W., and Callaway, J.L. (1984). Acne and Accutane. N. C. Med. J. 45(8): 513.
Business Wire. (2026). Thetis Pharmaceuticals. Company announcement: Thetis Pharmaceuticals presents new preclinical and clinical data for TP-317 at DDW 2025. https://www.businesswire.com/news/home/20250505954671/en/Thetis-Pharmaceuticals-Presents-New-Preclinical-and-Clinical-Data-forTP-317. Accessed 4 Feb. 2026.
Byrne, L., and Guiry, P.J. (2024). Advances in the chemistry and biology of specialized pro-resolving mediators (SPMs). Molecules. 29(10): 2233.
Chateauvieux, S., Morceau, F., Dicato, M., and Diederich, M. (2010). Molecular and therapeutic potential and toxicity of valproic acid. J. Biomed. Biotechnol 2010: 479364.
Chen, Y., Wu, X., Li, J., Ren, Y., Miao, H., Zhai, X., Huang, C., and Chen, X. (2025). Mechanisms of specialized pro-resolving mediators in pain relief. Front. Immunol. 16: 1634724.
Cheng, S., Wang, G., and Wang, X. (2019). Fatty acid oxidation inhibitor etomoxir suppresses tumour progression. Clin. Sci. 133(15): 1745–1758.
Chiang, N., and Serhan, C.N. (2020). Specialized pro-resolving mediator network. Essays Biochem. 64(3): 443–462.
Christensen, R., Henry, E., Wiedmeier, S.E., Burnett, J., and Lambert, D.K. (2007). Identifying patients at high risk of parenteral nutrition-associated liver disease. J. Perinatol. 27(5): 284–290.
Cision Canada. (2026). HLS Therapeutics announces Health Canada approval of Nilemdo for the reduction of LDL cholesterol. https://www.newswire.ca/news-releases/hls-therapeutics-announces-health-canada-approval-of-nilemdo-r-for-the-reduction-of-ldl-cholesterol-in-canadians-at-risk-of-cardiovascular-disease-837557792.html. Accessed 3 Feb. 2026.
ClinCalc DrugStats. (2026). Bimatoprost. Drug Usage Statistics, United States, 2014-2023. https://clincalc.com/DrugStats/Drugs/Bimatoprost. Accessed 4 Feb. 2026.
Clouser, M.C., Roe, D.J., Foote, J.A., Harris, R.B., and Alberts, D.S. (2010). Dose response of retinol and isotretinoin. Nutr. Cancer. 62(8): 1058–1066.
DailyMed. (2026). Label: Bimatoprost solution/drops. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=27bef7e1-750a-4ac1-ab5f-e4c0121ffcbc. Accessed 6 Feb. 2026.
Davie, J.R. (2003). Inhibition of histone deacetylase activity by butyrate. J. Nutr. 133(7 Suppl): 2485S–2493S.
Deckelbaum, R.J., Zirpoli, H., Dahl, S.W., and Kralovec, J.A. (2024). Delivery systems for bioactive lipids. US 2024/0390502.
DeckTherapeutics. (2024). Company information. https://www.decktherapeutics.com/. Accessed 4 Feb. 2026.
Defraeye, T., Bahrami, F., Kowatsch, T., Annaheim, S., Bragt, M.C., Rossi, R.M., and Greger, M. (2025). Advances in food-as-medicine interventions. Adv. Nutr. 16(6): 100421.
Doggrell, S.A. (2004). ETC-588 (Pfizer). Curr. Opin. Investig. Drugs. 5: 993–999.
Dominiak, A., Chełstowska, B., and Nowicka, G. (2025). Metabolic Adaptations in cancer progression: optimization strategies and therapeutic targets. Cancers (Basel) 17(14): 2341.
Drees, B.M., and Barthel, B. (2022). We are what we eat. Mo. Med. 119(5): 479–480.
Drugs. (2026a). Valproic acid monograph. https://www.drugs.com/monograph/valproic-acid.html. Accessed 3 Feb. 2026.
Drugs. (2026b). Lovaza prescribing information. https://www.drugs.com/pro/lovaza.html. Accessed 4 Feb. 2026.
Drugs. (2026c). Alprostadil monograph. https://www.drugs.com/monograph/alprostadil-systemic-local.html. Accessed 7 Feb. 2026.
Drugs. (2026d). Misoprostol monograph. https://www.drugs.com/misoprostol.html. Accessed 4 Feb. 2026.
Drugs. (2026e). Bimatoprost monograph. https://www.drugs.com/monograph/bimatoprost.html. Accessed 4 Feb. 2026.
Drugs. (2026f). Latanoprost monograph. https://www.drugs.com/monograph/latanoprost.html. Accessed 4 Feb. 2026.
Drugs. (2026g). Epoprostenol monograph. https://www.drugs.com/monograph/epoprostenol.html. Accessed 4 Feb. 2026.
Drugs. (2026h). Illoprost pulmonary hypertension/oral inhalation monograph. https://www.drugs.com/monograph/iloprost-pulmonary-hypertension-oral-inhalation.html.
Drugs. (2026i). Tretinoin monograph. https://www.drugs.com/tretinoin.html. Accessed 4 Feb. 2026.
Dudzinski, D.M., and Serhan, C.N. (2017). Pharmacology of eicosanoids. In: Golan, D.E., Armstrong, E.J., and Armstrong, A.W. (Ed.). Principles of Pharmacology: The pathophysiologic basis of drug therapy. (4th ed.). Wolters Kluwer, Philadelphia, PA, pp. 781–796.
EMA (European Medicines Agency). (2026a). alproate: Direct healthcare professional communication. https://www.ema.europa.eu/en/medicines/dhpc/valproate. Accessed 3 Feb. 2026.
EMA (European Medicines Agency). (2026b). Nilemdo: European public assessment report. https://www.ema.europa.eu/en/medicines/human/EPAR/nilemdo. Accessed 3 Feb. 2026.
EMA (European Medicines Agency). (2026c). Catiolanze EPAR. https://www.ema.europa.eu/en/medicines/human/EPAR/catiolanze. Accessed 4 Feb. 2026.
EMA (European Medicines Agency). (2026d). Ventavis EPAR. https://www.ema.europa.eu/en/medicines/human/EPAR/ventavis. Accessed 4 Feb. 2026.
EMA (European Medicines Agency). (2026e). Trepulmix EPAR. https://www.ema.europa.eu/en/medicines/human/EPAR/trepulmix. Accessed 4 Feb. 2026.
Escriba-Ruiz, P.V., Barceló-Coblijn, G., Martín, M.L., Teres-Jiménez, S., Noguera-Salva, M.A., Busquets-Xaubet, X., López-Jiménez, D., Ibarguren-Aizpitarte, M., Soto-Salvador, J.J., and Yus-Astiz, M. (2013). Enantiomers of 2-hydroxy derivatives of fatty acids. WO2013/050644.
Essentiale. (2026). Essentiale® Forte P: Accelerate liver regeneration. Product Information. https://www.essentiale.com/en-ph/products/essentiale-forte. Accessed 3 Feb. 2026.
Fahy, E., Subramaniam, S., Murphy, R., Nishijima, M., Raetz, C., Shimizu, T., Spener, F., van Meer, G., Wakelam, M., and Dennis, E.A. (2009). Update of the LIPID MAPS classification system. J. Lipid Res. 50(Suppl.): S9–S14.
FemTech Canada. (2026). SPM Therapeutics Inc. Company information. https://femtech.ca/company/spm-therapeutics-inc/. Accessed 4 Feb. 2026.
Fialkow, J. (2016). Omega-3 fatty acid formulations in cardiovascular disease: Dietary supplements are not substitutes for prescription prod-

ucts. Am. J. Cardiovasc. Drugs. 16(4): 229–239.
Finanger, E., Vandenborne, K., Finkel, R.S., Sweeney, H.L., Tennekoon, G., Yum, S., Mancini, M., Bista, P., Nichols, A., Liu, H., Fretzen, A., and Donovan, J.M. (2019). Phase 1 study of edasalonexent. J. Neuromuscul. Dis. 6(1): 43–54.
Finkel, R.S., McDonald, C.M., Lee Sweeney, H., Finanger, E., Neil Knierbein, E., Wagner, K.R., Mathews, K.D., Marks, W., Statland, J., Nance, J., McMillan, H.J., McCullagh, G., Tian, C., Ryan, M.M., O'Rourke, D., Müller-Felber, W., Tulinius, M., Burnette, W.B., Nguyen, C.T., Vijayakumar, K., Johannsen, J., Phan, H.C., Eagle, M., MacDougall, J., Mancini, M., Donovan, J.M., and For the PolarisDMD Study Group. (2021). A Randomized, double-blind, placebo-controlled, global Phase 3 study of edasalonexent in pediatric patients with Duchenne Muscular Dystrophy: Results of the PolarisDMD trial. J. Neuromuscul. Dis. 8(5): 769–784.
Flores, J., White, B.M., Brea, R.J., Baskin, J.M., and Devaraj, N.K. (2020). Lipids: Chemical tools for synthesis and analysis. Chem. Soc. Rev. 49(14): 4602–4614.
Fredman, G., and Serhan, C.N. (2024). Specialized pro-resolving mediators in vascular inflammation. Nat. Rev. Cardiol. 21(11): 808–823.
Fresenius Kabi. (2026). Fresenius Kabi Announces U.S. Availability of Omegaven® (fish oil triglycerides) injectable emulsion. https://www.fresenius-kabi.com/us/news-and-events/fresenius-kabi-announces-u-s--availability-of-omegaven---fish-oil. Accessed 8 Feb. 2026.
Gao, W., Guo, L., Yang, Y., Wang, Y., Xia, S., Gong, H., Zhang, B.K., and Yan, M. (2022). Crosstalk between Nrf2 and NF-κB pathways in drug-induced toxicity. Front. Cell Dev. Biol. 9: 809952.
Ghasri, P., Yentzer, B.A., Dabade, T.S., and Feldman, S.R. (2011). Acitretin for the treatment of psoriasis: An assessment of national trends. J. Drugs Dermatol. 10(8): 876–880.
Ghodke-Puranik, Y., Thorn, C.F., Lamba, J.K., Leeder, J.S., Song, W., Birnbaum, A.K., Altman, R.B., and Klein, T.E. (2013). Valproic acid pathway: Pharmacokinetics and pharmacodynamics. Pharmacogenet. Genomics. 23(4): 236–241.
GISSI, GISSI-Prevenzione Investigators. (1999). Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Lancet 354: 447–455.
Global Growth Insights. (2026). Prostaglandin market report. https://www.globalgrowthinsights.com/market-reports/prostaglandin-market-121902. Accessed 4 Feb. 2026.
GlobeNewswire. (2026a). Acne drugs market size report. https://www.globenewswire.com/news-release/2023/06/07/2684073/0/en/Acne-Drugs-Market-Size-to-Reach-impressive-USD-15-2-Billion-by-2032-Says-Acumen-Research-and-Consulting.html. Accessed 4 Feb. 2026.
Gjorstrup, P., and Schwartz, E. (2010). Compositions and methods for the treatment of inflammation. WO2010/120719.
Gomberg-Maitland, M., and Olschewski, H. (2008). Prostacyclin therapies for the treatment of pulmonary arterial hypertension. Eur. Resp. J. 31(4): 891–901.
GrandView Research. (2026). Omega 3 prescription drug market outlook. https://www.grandviewresearch.com/horizon/outlook/omega-3-prescription-drugs-market/north-america. Accessed 4 Feb. 2026.
Guenther, L.C., Kunynetz, R., Lynde, C.W., Sibbald, R.G., Toole, J., Vender, R., and Zip, C. (2017). Acitretin use in dermatology. J. Cutan. Med. Surg. 21(3 Suppl): 2S–12S.
Gura, K.M., Duggan, C.P., Collier, S.B., Jennings, R.W., Folkman, J., Bistrian, B.R., and Puder, M. (2006). Reversal of parenteral nutrition-associated liver disease using parenteral fish oil. Pediatrics. 118(1): e197–201.
Hanchanale, V., and Eardley, I. (2014). Alprostadil for the treatment of impotence. Expert Opin. Pharmacother. 15(3): 421–428.
Hannun, Y.A., and Obeid, L.M. (2018). Sphingolipids and their metabolism in physiology and disease. Nat. Rev. Mol. Cell Biol. 19(3): 175–191.
Harris, E. (2024). FDA Approves Iloprost as First Drug to Treat Severe Frostbite. JAMA 331(11): 907.
Harris, W.S. (2019). Understanding why REDUCE-IT was positive - mechanistic overview of eicosapentaenoic acid. Prog. Cardiovasc. Dis. 62(5): 401–405.
Harrison, S.A., Alkhouri, N., Ortiz-Lasanta, G., Rudraraju, M., Tai, D., Wack, K., Shah, A., Besuyen, R., Steineger, H.H., Fraser, D.A., Sanyal, A.J., and ICONA Study Investigators. (2025). FFAR1/FFAR4 agonist icosabutate in MASH. J. Hepatol. 83(2): 293–303.
Hashimoto, M., and Hossain, S. (2018). Fatty acids: From membrane ingredients to signalling molecules. In: Waisundara, W. (Ed.). Biochemistry and health benefits of fatty acids. IntechOpen, (online resource), pp 1-20. https://www.intechopen.com/chapters/63324. Accessed 4 Feb. 2026.
Health Canada. (2015). New drug authorizations 2015: Highlights. https://www.canada.ca/en/health-canada/services/publications/drugs-health-products/health-canada-new-drug-authorizations-2015-highlights.html. Accessed 4 Feb. 2026.
Heckel, S., Favre, R., Weber, P., and Dellenbach, P. (1993). Tératogénicité des rétinoïdes. Un cas et revue de la littérature [Teratogenicity of retinoids. A case and review of the literature]. J. Gynecol. Obstet. Biol. Reprod. (Paris) 22(1): 43–7.
Hilleman, D.E., Wiggins, B.S., and Bottorff, M.B. (2020). Critical differences between dietary supplement and prescription omega-3 fatty acids: A narrative review. Adv. Ther. 37(2): 656–670.
Holubarsch, C.J., Rohrbach, M., Karrasch, M., Boehm, E., Polonski, L., Ponikowski, P., and Rhein, S.A. (2007). Double-blind randomized multicentre clinical trial to evaluate the efficacy and safety of two doses of etomoxir in comparison with placebo in patients with moderate congestive heart failure: The ERGO (etomoxir for the recovery of glucose oxidation) study. Clin. Sci. (Lond) 113(4): 205–212.
Hudson Jones, A. (2000). Medicine and the movies: Lorenzo's Oil at century's end. Ann. Intern. Med. 133(7): 567–571.
ICH GCP (International Conference on Harmonization, Good Clinical Practice). (2024). OMT-28 in patients with primary mitochondrial disease (PMD) (PMD-OPTION). Clinical trials registry: NCT05972954. https://ichgcp.net/clinical-trials-registry/NCT05972954. Accessed 4 Feb. 2026.
In Clinical Trials. (2026). Atrial fibrillation trial NCT03906799. https://inclinicaltrials.com/atrial-fibrillation/NCT03906799/. Accessed 4 Feb. 2026.
Jannas-Vela, S., Candia, A.A., Peñailillo, L., Barrios-Troncoso, P., Zapata-Urzúa, J., Rey-Puente, J., Aukema, H.M., Mutch, D.M., Valenzuela, R., and Valladares-Ide, D. (2023). Specialized pro-resolving mediators after omega-3 supplementation and exercise in rheumatoid arthritis. F1000Res. 12: 942.
Johnson, R.A., Lincoln, F.H., Thompson, J.L., Nidy, E.G., Mizak, S.A., and Axen, U. (1977). Synthesis and stereochemistry of prostacyclin and 6-ketoprostaglandin F1α. J. Am. Chem. Soc. 99(12): 4182–4184.
Kapoor, K., Alfaddagh, A., Stone, N.J., and Blumenthal, R.S. (2021). Omega-3 fatty acid trial landscape. J. Clin. Lipidol. 15(4): 545–555.
Katz, J., Gold, S., Christian, V.J., and Martindale, R. (2025). Specialized pro-resolving mediators in inflammatory bowel disease. Curr. Gastroenterol. Rep. 27(1): 43.
Kawasaki, Y., Iwahori, Y., Chiba, Y., Mitsumoto, H., Kawasaki, T., Fujita, S., and Takahashi, Y. (2019). Efficacy of DHA and EPA on serum triglycerides: Systematic review. Int. J. Nutrition. 3(2): 22–40.
Kawczak, P., Feszak, I., Brzeziński, P., and Bączek, T. (2024). Structure–activity relationships of retinoids. Biomedicines. 12(5): 1059.
Keeley, E.C., Li, H.J., Cogle, C.R., Handberg, E.M., Merz, C.N.B., and Pepine, C.J. (2022). Specialized pro-resolving mediators in coronary microvascular dysfunction. Am. J. Cardiol. 162: 1–5.
Kirtland, S.J. (1988). Prostaglandin E1: A review. Prostaglandins Leukot. Essent. Fatty Acids. 32(3): 165–174.
Klek, S. (2016). Omega-3 fatty acids in modern parenteral nutrition. J. Clin. Med. 5(3): 34.
Koutoulogenis, G.S., and Kokotos, G. (2021). Nitro fatty acids (NO2-FAs): An emerging class. Molecules. 26(24): 7536.
Kralovec, J.A., Rolle, A., and Mugford, P.F. (2023). Process for the production of diglycerides. EP3802762B1.
Kruszynska, Y.T., and Sherratt, H.S. (1987). Glucose kinetics during etomoxir treatment. Biochem. Pharmacol. 36(22): 3917–3921.
Lacy, B.E. (2006). Lubiprostone for chronic constipation. Gastroenterol. Hepatol. (NY) 2(7): 483.
Landry, M.J., Ward, C.P., Cunanan, K.M., Durand, L.R., Perelman, D., Robinson, J.L., Hennings, T., Koh, L., Dant, C., Zeitlin, A., Ebel, E.R., Sonnenburg, E.D., Sonnenburg, J.L., and Gardner, C.D. (2023). Cardiometabolic effects of omnivorous vs vegan diets. JAMA Netw. Open. 6(11): e2344457.

Lang, L. (2008). The Food and Drug Administration approves lubiprostone for irritable bowel syndrome with constipation. Gastroenterology 135(1): 7.
Lederer, A.K., and Huber, R. (2022). The relation of diet and health. Int. J. Environ. Res. Public Health. 19(13): 7774.
Le Maire, A., Alvarez, S., Shankaranarayanan, P., Lera, A.R., Bourguet, W., and Gronemeyer, H. (2012). Retinoid receptors and therapeutic applications of RAR/RXR modulators. Curr. Top. Med. Chem. 12(6): 505–527.
Lewis, M. (2017). Intravenous omega-3 fatty acid compositions. US 9,675,572.
Lipid Maps. (2026). Lipid Maps Lipidomics Gateway. https://lipidmaps.org/. Accessed 4 Feb. 2026.
Lopaschuk, G.D., Belke, D.D., Gamble, J., Itoi, T., and Schönekess, B.O. (1994). Regulation of fatty acid oxidation in the mammalian heart in health and disease. Biochim. Biophys. Acta. 1213(3): 263–276.
Lovaza. (2026). Official product website. https://lovaza.com/. Accessed 4 Feb. 2026.
Luan, L., Frederick, N.P., and Baskin, J.M. (2025). Emerging approaches for studying lipid dynamics. Annu. Rev. Biochem. 94(1): 417–446.
Luczak, J.W., Palusińska, M., Maślińska-Gromadka, K., Pietrzak, D., Szopiński, T., Lewicki, S., Schenk, T., and Szymański, Ł. (2025). The Next Generation of Skin Care: Transforming retinoid therapeutics. Cells 14(21): 1650.
Maki, K.C., Bays, H.E., Ballantyne, C.M., Underberg, J.A., Kastelein, J.J.P., Johnson, J.B., and Ferguson, J.J. (2022). A head-to-head comparison of a free fatty acid formulation of omega-3 pentaenoic acids versus icosapent ethyl in adults with hypertriglyceridemia: The ENHANCE-IT study. J. Am. Heart Assoc. 11(6): e024176.
Maliha, A., Tahsin, M., Fabia, T.Z., Rahman, S.M., and Rahman, M.M. (2024). Pro-resolving metabolites: Future of the fish oil supplements. J. Funct. Foods. 121: 106439.
Maresins Biopharma. (2026). Targeted relief from chronic inflammation. Company information. https://www.maresinsbiopharma.com/. Accessed 4 Feb. 2026.
MarketUS. (2026). Omega-3 prescription drugs market report. https://market.us/report/omega-3-prescription-drugs-market/. Accessed 4 Feb. 2026.
Mayser, P., Grimm, H., and Grimminger, F. (2002). n-3 Fatty acids in psoriasis. Br. J. Nutr. 87(S1): S77–S82.
Mochel, F., DeLonlay, P., Touati, G., Brunengraber, H., Renee, P., Kinman, R.P., Rabier, D., Roe, C.R., and Saudubray, J.-M. (2005). Pyruvate carboxylase deficiency: Clinical and biochemical response to anaplerotic diet therapy. Mol. Genet. Metab. 84: 305–312.
Mohaibes, R.J., Fiol-deRoque, M.A., Torres, M., Ordinas, M., López, D.J., Castro, J.A., Escribá, P.V., and Busquets, X. (2017). The hydroxylated form of docosahexaenoic acid (DHA-H) modifies the brain lipid composition in a model of Alzheimer's disease, improving behavioural motor function and survival. Biochim. Biophys. Acta Biomembr. 1859(9 Pt B): 1596–1603.
Mohiuddin, A.K. (2019). A comprehensive review of acne vulgaris. J. Clin. Pharmacy. 1: 17–45.
Moncada, S., Gryglewski, R., Bunting, S., and Vane, J.R. (1976). An enzyme isolated from arteries transforms prostaglandin endoperoxides to an unstable substance that inhibits platelet aggregation. Nature. 263: 663–665.
Montemarano, M (2020). Will an EPA drug candidate be used to treat COVID-19? Nutraceutical World. https://www.nutraceuticalsworld.com/breaking-news/will-an-epa-drug-candidate-be-used-to-treat-covid-19/. Accessed 3 Feb. 2026.
Mordor Intelligence. (2026). Omega-3 prescription drug market. https://www.mordorintelligence.com/industry-reports/omega-3-prescription-drugs-market. Accessed 3 Feb. 2026.
Muscular Dystrophy News. (2026). Edasalonexent. https://musculardystrophynews.com/edasalonexent/. Accessed 3 Feb. 2026.
Nichols, S.J., Lincoff, A.M., Garcia, M., Bash, D., Ballantyne, C.M., Barter, P.J., Davidson, M.H., Kastelein, J.J.P., Koenig, W., McGuire, D.K., Mozaffarian, D., Ridker, P.M., Ray, K.K., Katona, B.G., Himmelmann, A., Loss, L.E., Rensfeldt, M., Lundström, T., Agrawal, R., Menon, V., Wolski, K., and Nissen, S.E. (2020). Effect of high-dose omega-3 fatty acids vs corn oil on major adverse cardiovascular events. The STRENGTH randomized clinical trial. JAMA 324(22): 2268–2280.
Nichols, W. (2022). DSM fills fish-alternative nutrient gap with EU-approved omega-3 derived from algae. NutritionInsight. https://www.nutritioninsight.com/news/dsm-fills-fish-alternative-nutrient-gap-with-eu-approved-omega-3-derived-from-algae.html. Accessed 3 Feb. 2026.
NIH. (2026a). ClinicalTrials.gov. Effects of oral sodium butyrate supplementation on body weight reduction in overweight/obese individuals with and without type 2 diabetes (ButRed). Study record NCT07252609. https://clinicaltrials.gov/study/NCT07252609. Accessed 3 Feb. 2026.
NIH. (2026b). ClinicalTrials.gov. A Phase III trial of Lorenzo's oil in adrenomyeloneuropathy. Study record NCT00545597. https://clinicaltrials.gov/study/NCT00545597. Accessed 3 Feb. 2026.
NIH. (2026c). ClinicalTrials.gov. Expanded access for Lorenzo's oil (GTO/GTE) in adrenoleukodystrophy. Study record NCT02233257. https://clinicaltrials.gov/study/NCT02233257. Accessed 3 Feb. 2026.
NIH. (2026d). ClinicalTrials.gov. LAM561 with RT and TMZ for adults with glioblastoma (CLINGLIO). Study record NCT04250922. https://clinicaltrials.gov/study/NCT04250922. Accessed 8 Feb. 2026.
NIH. (2026e). ClinicalTrials.gov. FIRSTx - A study of oral CXA-10 in primary focal segmental glomerulosclerosis (FSGS). Study record NCT03422510. https://clinicaltrials.gov/study/NCT03422510. Accessed 3 Feb. 2026.
NIH. (2026f). ClinicalTrials.gov. Effect of EPA-FFA on polypectomy in familial adenomatous polyposis. Study record NCT03806426. https://clinicaltrials.gov/study/NCT03806426. Accessed 3 Apr. 2026.
NIH. (2026g). ClinicalTrials.gov. EPA-FFA to treat hospitalized patients with COVID-19 (SARS-CoV-2). Study Record NCT04335032. https://clinicaltrials.gov/study/NCT04335032. Accessed 6 Feb. 2026.
NIH. (2026h). ClinicalTrials.gov. Pharmacodynamic effects of a free-fatty acid formulation of omega-3 pentaenoic acid in adults with hypertriglyceridemia (ENHANCE-IT). Study record NCT04177680. https://www.clinicaltrials.gov/NCT04177680. Accessed 3 Feb. 2026.
NIH. (2026i). ClinicalTrials.gov. (2022). Phase III study of edasalonexent in boys with Duchenne Muscular Dystrophy (PolarisDMD). Study record NCT03703882. https://clinicaltrials.gov/study/NCT03703882. Accessed 3 Feb. 2026.
NIH. (2026j). ClinicalTrials.gov. (2025). Mechanisms of prognostic regulation and precision phenotype identification in severe infections driven by specialized pro-resolving mediators (MPR-PPI-SPMs). Study record NCT07353970. https://clinicaltrials.gov/study/NCT07353970. Accessed 4 Feb. 2026.
Nissen, S.E., Wolski, K., and Topol, E.J. (2005). Effect of muraglitazar on death and major adverse cardiovascular events in patients with type 2 diabetes mellitus. JAMA 294(20): 2581–2586.
Oniciu, D.C., and Dasseux, J.-L.H. (2004). Hydroxyl compounds and compositions for cholesterol management and related uses. WO 2004067489.
Ortner, V.K., Johansen, B., Kilov, K., Castillo-Mondragón, A., Duvold, T., Kihl, J., Ashcroft, F.J., Feuerherm, A.J., Pind Laugesen, C., Marcker Espersen, M.L., Manole, I., Isberg, A.P., Andersen, A.D., Rakvaag, E., Zibert, J.R., and Haedersdal, M. (2022). The Copenhagen Actinic Keratosis Study (COAKS). BMJ Open. 5(12): e061012.
Padayachee, L., Kale, M., Mannerfeldt, J., and Metcalfe, A. (2020). Oral misoprostol for induction of labour in term PROM: A systematic review. J. Obstet. Gynaecol. Can. 42(12): 1525–1531.
Parets, S., Irigoyen, Á., Ordinas, M., Cabot, J., Miralles, M., Arbona, L., Péter, M., Balogh, G., Fernández-García, P., Busquets, X., Lladó, V., and Torres, M. (2020). 2-Hydroxy-docosahexaenoic acid conversion via α-oxidation. Front. Cell Dev. Biol. 8: 164.
Patel, S.S., and Spencer, C.M. (1996). Latanoprost: Pharmacological properties and clinical efficacy. Drugs Aging 9: 363–378.
Patil, A.J., Vajaranant, T.S., and Edward, D.P. (2009). Bimatoprost: A review. Expert Opin. Pharmacother. 10(16): 2759–2768.
Paton, D.M. (2017). Bempedoic acid: ATP-citrate lyase inhibitor. Drugs Fut. 42: 201–208.
Patted, P.G., Masareddy, R.S., Patil, A.S., Kanabargi, R.R., and Bhat, C.T. (2024). Omega-3 fatty acids: Comprehensive scientific review. Futur. J. Pharm. Sci. 10: 94.
Pedersen, J., Hedegaard, B.S., Schmidt, E.B., Dahm, C.C., Holven, K.B., Retterstøl, K., Calder, P.C., and Bork, C. (2025). Monounsaturated fatty acids in cardiovascular disease. Nutrients 17(15): 2509.

PHA (Pulmonary Hypertension Association). (2026). Tyvaso (oral inhaled treprostinil). PHA document. https://phassociation.org/pulmonary-hypertension/treatments/targeted-therapies/tyvaso/. Accessed 7 Feb 2026.

Pinkosky, S.L., Newton, R.S., Day, E.A., Ford, R.J., Lhotak, S., Austin, R.C., Birch, C.M., Smith, B.K., Filippov, S., Groot, P.H.E., Steinberg, G.R., and Lalwani, N.D. (2016). Liver-specific ATP-citrate lyase inhibition by bempedoic acid decreases LDL-C and attenuates atherosclerosis. Nat. Commun. 7: 13457.

Pluchart, H., Khouri, C., Blaise, S., Roustit, M., and Cracowski, J.L. (2017). Targeting the prostacyclin pathway: Beyond pulmonary arterial hypertension. Trends Pharmacol. Sci. 38(6): 512–523.

PMDA (Pharmaceuticals and Medical Devices Agency). (2020). Summary of investigation results ethyl icosapentate omega-3-acid ethyl esters. https://www.pmda.go.jp/files/000271892.pdf. Accessed 3 Feb. 2026.

Precedence Research. (2026a). Prostaglandin analogs market. https://www.precedenceresearch.com/prostaglandin-analogs-market. Accessed 4 Feb. 2026.

Precedence Research. (2026b). Vitamin D market. https://www.precedenceresearch.com/vitamin-d-market. Accessed 3 Feb. 2026.

PR Newswire. (2026a). Laminar Pharma releases first progression-free survival data for LAM561 in newly diagnosed glioblastoma therapy. https://www.prnewswire.com/news-releases. Accessed 6 Feb. 2026.

PR Newswire. (2026b). Ability Pharmaceuticals: Company news. https://www.prnewswire.com/news-releases/ability-pharmaceuticals. Accessed 3 Feb. 2026.

PR Newswire. (2026c). US Food and Drug Administration. The FDA approves the use of the drug to reduce the risk of cardiovascular events in certain adult patient groups. https://www.prnewswire.com/news-releases/fda-approves-use-of-drug-to-reduce-risk-of-cardiovascular-events-in-certain-adult-patient-groups-300974813.html. Accessed 3 Feb. 2026.

Rahmani, D., Chodari, L., Kakallahpour, M., and Niknam, Z. (2025). Therapeutic potential of sodium butyrate in neurological and psychiatric disorders. Mol. Neurobiol. 63: 90.

Rare Cancer News. (2026). The LAM 561 combination may delay glioblastoma progression. https://rarecancernews.com/news/lam561-combination-delay-glioblastoma-disease-progression/. Accessed 4 Feb. 2026.

Resul, B., Stjernschantz, J., No, K., Liljebris, C., Selén, G., Astin, M., Karlsson, M., and Bito, L.Z. (1993). Phenyl-substituted prostaglandins: Potent antiglaucoma agents. J. Med. Chem. 36(2): 243–248.

Roe, C.R., and Mochel, F. (2006). Anaplerotic diet therapy in inherited metabolic disease: Therapeutic potential. J. Inherit. Metab. Dis. 29(2-3): 332–340.

Roe, C.R., Yang, B.Z., Brunengraber, H., Roe, D.S., Wallace, M., and Garritson, B.K. (2008). Carnitine palmitoyltransferase II deficiency: Successful anaplerotic diet therapy. Neurology. 22: 260–264.

Rondina, M.T. (2023). Targeting prostacyclin: All gain with no pain? Blood 142(18): 1506–1507.

Roos, J., Manolikakes, G., Schlomann, U., Klinke, A., Schopfer, F.J., Neumann, C.A., and Maier, T.J. (2024). Nitro-fatty acids as cancer therapeutics. Trends Pharmacol. Sci. 45(11): 1061–1080.

Rosell, R. (2025). Concerns about induction of autophagy: À propos of ibrilatazar. Lung Cancer 205: 108619.

RSC (Royal Society of Chemistry). (2026). Butyric acid: chemical profile [Internet]. London: RSC Education; c2020– [cited 2026 Apr 5]. https://edu.rsc.org/resources/butyric-acid/4012185. Accessed 5 Apr. 2026.

Ruopp, N.F., and Cockrill, B.A. (2022). Diagnosis and treatment of pulmonary arterial hypertension: A review. JAMA 327(14): 1379–1391.

Saidaiah, P., Banu, Z., Khan, A.A., Geetha, A., and Somraj, B. (2024). Comprehensive review of omega-3 fatty acids. Ann. Phytomed. 13(1): 209–225.

Santos, R., Linker, S.B., Stern, S., Mendes, A.P.D., Shokhirev, M.N., Erikson, G., Randolph-Moore, L., Racha, V., Kim, Y., Kelsoe, J.R., Bang, A.G., Alda, M., Marchetto, M.C., and Gage, F.H. (2021). Deficient LEF1 expression is associated with lithium resistance and hyperexcitability in neurons derived from bipolar disorder patients. Mol. Psychiatry. 26: 2440–2456.

Schopfer, F.J., Vitturi, D.A., Jorkasky, D.K., and Freeman, B.A. (2018). Nitro-fatty acids: New drug candidates. Nitric Oxide. 79: 31–37.

Scott, J.S., Nassar, Z.D., Swinnen, J.V., and Butler, L.M. (2022). Monounsaturated fatty acids: Key regulators of cell viability and intracellular signalling in cancer. Mol. Cancer Res. 20(9): 1354–1364.

Shapiro, L.S., Toledo-Garcia, A.E., and Farrell, J.F. (2013). Treatment of malignant atrophic papulosis with treprostinil. Orphanet J. Rare Dis. 8: 52.

Shingari, M., Sharma, A., and Mittal, V. (2025). Nature's Remedy: A comprehensive review exploring herbal treatments and natural approaches for preventing acne vulgaris. Recent Adv. Antiinfect. Drug Discov. 21(1): 1–26.

Shirley, M. (2020). Triheptanoin: First approval. Drugs 80(15): 1595–1600.

Shroot, B. (1986). Pharmacology of topical retinoids. J. Am. Acad. Dermatol. 15(4Pt2): 748–56.

Siddiqui, Z., Zufall, A., Nash, M., Rao, D., Hirani, R., and Russo, M. (2024). Comparing tretinoin to other topical therapies in photoaging. Am. J. Clin. Dermatol. 25(6): 873–890.

Singh, D., Gupta, S., Verma, I., Morsy, M.A., Nair, A.B., and Ahmed, A.-S.F. (2021). Hidden pharmacological activities of valproic acid: A new insight. Biomed. Pharmacother. 142: 112021.

Skulas-Ray, A.C., Wilson, P.W.F., Harris, W.S., Brinton, E.A., Kris-Etherton, P.M., Richter, C.K., Jacobson, T.A., Engler, M.B., Miller, M., Robinson, J.G., Blum, C.B., Rodriguez-Leyva, D., de Ferranti, S.D., Welty, F.K., and AHA Councils. (2019). Omega-3 fatty acids for hypertriglyceridemia. Circulation 140(12): e673–e691.

Sneader, W. (2005). Drug Discovery: A History. John Wiley & Sons, Chichester, UK, p. 185.

Sousa, A.B., and Barbosa, J.N. (2023). The use of specialized pro-resolving mediators in biomaterial-based immunomodulation. J. Funct. Biomater. 14(4): 223.

Sridharan, K. (2024). Systemic adverse drug events to topical prostaglandin analogs for treating glaucoma: a retrospective focused pharmacovigilance study. BMC Ophthalmol. 24(1): 554–564.

Stitham, J., Midgett, C., Martin, K.A., and Hwa, J. (2011). Prostacyclin: An inflammatory paradox. Front. Pharmacol. 2: 24.

Stjernschantz, J., and Alm, A. (1996). Latanoprost in glaucoma management. Curr. Opin. Ophthalmol. 7(2): 11–17.

Synapse. (2026). Drug profile: ETC-588. https://synapse.patsnap.com/drug/34ca054bec6443c09b24da3c%b16c6d98. Accessed 4 Feb. 2026.

Tavazzi, L., Tognoni, G., Franzosi, M.G., Latini, R., Maggioni, A.P., Marchioli, R., Nicolosi, G.L., Porcu, M., and GISSI-HF Investigators. (2004). Rationale and design of the GISSI heart failure trial: a large trial to assess the effects of n-3 polyunsaturated fatty acids and rosuvastatin in symptomatic congestive heart failure. Eur. J. Heart. Fail. 6(5): 635–641.

Thetis Pharmaceuticals. (2021). Company announcement. https://www.thetispharma.com/news/2021-08-23-585gw. Accessed 4 Feb. 2026.

Thetis Pharmaceuticals. (2024). Company news. https://www.thetispharma.com/news/2024-01-16-63lwl. Accessed 4 Feb. 2026.

Toncan, F., Raj, R.R., and Lee, M.J. (2025). Dynamics of fatty acid composition in lipids and their distinct roles in cardiometabolic health. Biomolecules 15(5): 696.

Torres, F., and Rubin, L.J. (2013). Treprostinil for the treatment of pulmonary arterial hypertension. Expert Rev. Cardiovasc. Ther. 11(1): 13–25.

Torricelli, A.A., Santhanam, A., Agrawal, V., and Wilson, S.E. (2014). Resolvin E1 analog RX-10045 reduces corneal stromal haze after PRK in rabbits. Mol. Vis. 20: 1710–1716.

Torgersen, M.L., Klokk, T.I., Kavaliauskiene, S., Klose, C., Simons, K., Skotland, T., and Sandvig, K. (2016). The anti-tumor drug 2-hydroxyoleic acid stimulates signalling and retrograde transport. Oncotarget 7: 86871–86888.

Touyz, R.M. (2024). Pharmacology and precision medicine: Preparing for the next era in clinical medicine. Editorial. Pharmacol. Rev. 76(4): 559–560.

Tripathy, K., Patel, P., and Geetha, R. (2024). Latanoprost. Stat Pearls Publishing, Treasure Island, FL, https://www.ncbi.nlm.nih.gov/books/NBK541062/. Accessed 28 Feb. 2026.

Tsutsumi, R., Yamasaki, Y., Takeo, J., Miyahara, H., Sebe, M., Bando, M., Tanba, Y., Mishima, Y., Takeji, K., Ueshima, N., Kuroda, M., Masumoto, S., Harada, N., Fukuda, D., Yoshimoto, R., Tsutsumi, Y.M., Aihara,

K.I., Sata, M., and Sakaue, H. (2021). Long-chain monounsaturated fatty acids improve endothelial function with altering microbial flora. Transl. Res. 237: 16–30.

US FDA. (2026a). Valproate information. https://www.fda.gov/drugs/post-market-drug-safety-information-patients-and-providers/valproate-information. Accessed 3 Feb. 2026.

US FDA. (2026b). Dojolvi, NDA 213687: Drug approval package. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&pApplNo=213687. Accessed 3 Feb. 2026.

US FDA. (2026c). Nexletol. NDA 211616: Original approval package. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/211616Orig1s000TOC.cfm. Accessed 3 Feb. 2026.

US FDA. (2026d). Drug trials snapshots: Nexletol. https://www.fda.gov/drugs/resources-information-approved-drugs/drug-trials-snapshots-nexletol. Accessed 3 Feb. 2026.

US FDA. (2026e). Amitiza (Lubiprostone), NDA 021908: Drug Approval Package. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2006/021908s000_AmitizaTOC.cfm. Accessed 7 Feb. 2026.

US FDA. (2026f). Draft Guidance on Omega-3-Acid Ethyl Esters Type A. October 2024. https://www.accessdata.fda.gov/drugsatfda_docs/psg/PSG_204977.pdf. Accessed 7 Feb. 2026.

US Pharmacist. (2026). AHA issues new scientific advisory on prescription omega-3 fatty acid benefits. https://www.uspharmacist.com/article/aha-issues-new-scientific-advisory-on-prescription-omega3-fattyacid-benefits/. Accessed 3 Feb. 2026.

Uzuncakmak, T.K., and Karadag, A.S. (2019). Mucocutaneous side effects. In: Karadag, A.S., Aksoy, B., and Parish, L.C. (Ed.). Retinoids in dermatology. 1st edition. CRC Press, Boca Raton, FL, pp. 95–104.

van Meer, G., Voelker, D.R., and Feigenson, G.W. (2008). Membrane lipids: Where they are and how they behave. Nat. Rev. Mol. Cell Biol. 9(2): 112.

Vernia, P., Fracasso, P.L., Casale, V., Villotti, G., Marcheggiano, A., Stigliano, V., Pinnaro, P., Bagnardi, V., and Caprilli, R. (2000). Topical butyrate for acute radiation proctitis: randomised, crossover trial. Lancet. 356(9237): 1232–1235.

Wang, Z., Yang, Y., Tang, F., and Wu, M. (2024). Recent applications and prospects of omega-3 fatty acids: A bibliometric study and visualization analysis in 2014–2023. Prostaglandins Leukot. Essent. Fatty Acids. 201: 102615.

Webster, L.R., Brewer, R.P., Lichtlen, P., Losch-Beridon, T., Mareya, S., and Wang, M. (2018). Efficacy of lubiprostone for the treatment of opioid-induced constipation, analyzed by opioid class. Pain Med. 19: 1195–1205.

Weiss, J.S., Ellis, C.N., Headington, J.T., Tincoff, T., Hamilton, T.A., and Voorhees, J.J. (1988). Topical tretinoin improves photoaged skin. A double-blind vehicle-controlled study. JAMA 259(4): 527–32.

Wenk, M.R. (2005). The emerging field of lipidomics. Nat. Rev. Drug Discov. 4(7): 594–610.

West, N.J., Clark, S.K., Phillips, R.K., Hutchinson, J.M., Leicester, R.J., Belluzzi, A., and Hull, M.A. (2010). Eicosapentaenoic acid reduces rectal polyp number and size in familial adenomatous polyposis. Gut 59(7): 918–25.

WHO. (2026a). Topics: Nutrition. https://www.who.int/health-topics/nutrition#tab=tab_1. Accessed 4 Feb. 2026.

WHO. (2026b). World Health Organization Model List of Essential Medicines: 21st List 2019. Geneva: World Health Organization. https://www.who.int/publications/i/item/WHOMVPEMPIAU2019.06. Accessed 4 Feb. 2026.

WHO. (2026c). The Selection and Use of Essential Medicines 2023: Web Annex A. Geneva: World Health Organization. https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.02. Accessed 4 Feb. 2026.

Woodcock, S.R., Bonacci, G., Gelhaus, S.L., and Schopfer, F.J. (2013). Nitrated fatty acids: Synthesis and measurement. Free Radic. Biol. Med. 59: 14–26.

Woodward, D.F., Andrews, S.W., Burk, R.M., and Garst, M.E. (1994). Non-acidic cyclopentane heptanoic acid derivatives as therapeutic agents. WO199406433.

Xu, R., Zhang, L., Pan, H., and Zhang, Y. (2024). Retinoid X receptor heterodimers in hepatic function: Structural insights and therapeutic potential. Front. Pharmacol. 15: 1464655.

Yoham, A.L., and Casadesus, D. (2023). Tretinoin. Stat Pearls Publishing, Treasure Island, FL, https://www.ncbi.nlm.nih.gov/books/NBK557478/. Accessed 4 Feb. 2026.

Yokoyama, M., Origasa, H., Matsuzaki, M., Matsuzawa, Y., Saito, Y., Ishikawa, Y., Oikawa, S., Sasaki, J., Hishida, H., Itakura, H., Kita, T., Kitabatake, A., Nakaya, N., Sakata, T., Shimada, K., Shirato, K., and Japan EPA lipid intervention study (JELIS) investigators. (2007). Effects of eicosapentaenoic acid on major coronary events in hypercholesterolaemic patients (JELIS): A randomized open-label, blinded endpoint analysis. Lancet 369: 1090–1098.

Zhang, H., and Xu, X. (2025). Nutritional lipids: Overview of nutritional progress and market trends. J. Food Bioact. 31: 8–30.

Zhou, L., Zhan, W., and Wei, X. (2022). Clinical pharmacology and pharmacogenetics of prostaglandin analogues in glaucoma. Front. Pharmacol. 13: 1015338.

Zirpoli, H., Bernis, M.E., Sabir, H., Manual Kollareth, D.J., Hamilton, J.A., Huang, N., Ng, J., Sosunov, S.A., Gaebler, B., Ten, V.S., and Deckelbaum, R.J. (2024). Omega-3 diglyceride emulsions as injectable therapeutics. Biomed. Pharmacother. 175: 116749.

Zirpoli, H., Chang, C.L., Carpentier, Y.A., Michael-Titus, A.T., Ten, V.S., and Deckelbaum, R.J. (2020). Novel approaches for omega-3 therapeutics. Annu. Rev. Nutr. 40: 161–187.

Zito, P.M., and Mazzoni, T. (2021). Acitretin. Stat Pearls Publishing, Treasure Island, FL, https://www.ncbi.nlm.nih.gov/books/NBK519571/. Accessed 4 Feb. 2026.