Product Pipeline

Overview

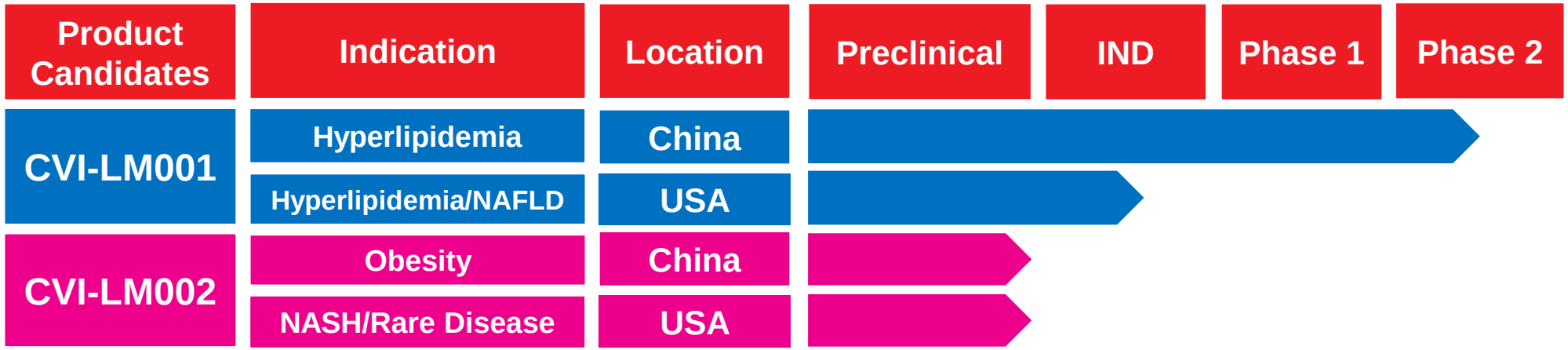
CVI Pharmaceuticals is advancing a clinical stage pipeline to address the unmet medical needs in hypercholesterolemia and complex medical challenges of patients in liver and rare metabolic diseases.

Standard of Care lipid-lowering statins are effective at lowering LDL-cholesterol (LDL-C), leading to well-documented CV benefits. However, not all patients can tolerate statins or reach their LDL-C goal on maximally-tolerated statin-dosing. Patients with atherosclerotic cardiovascular disease (ASCVD) or heterozygous familial hypercholesterolemia (HeFH) who require additional LDL-C lowering on top of maximally-tolerated statin therapy represent a high-risk patient population with an unmet medical need.

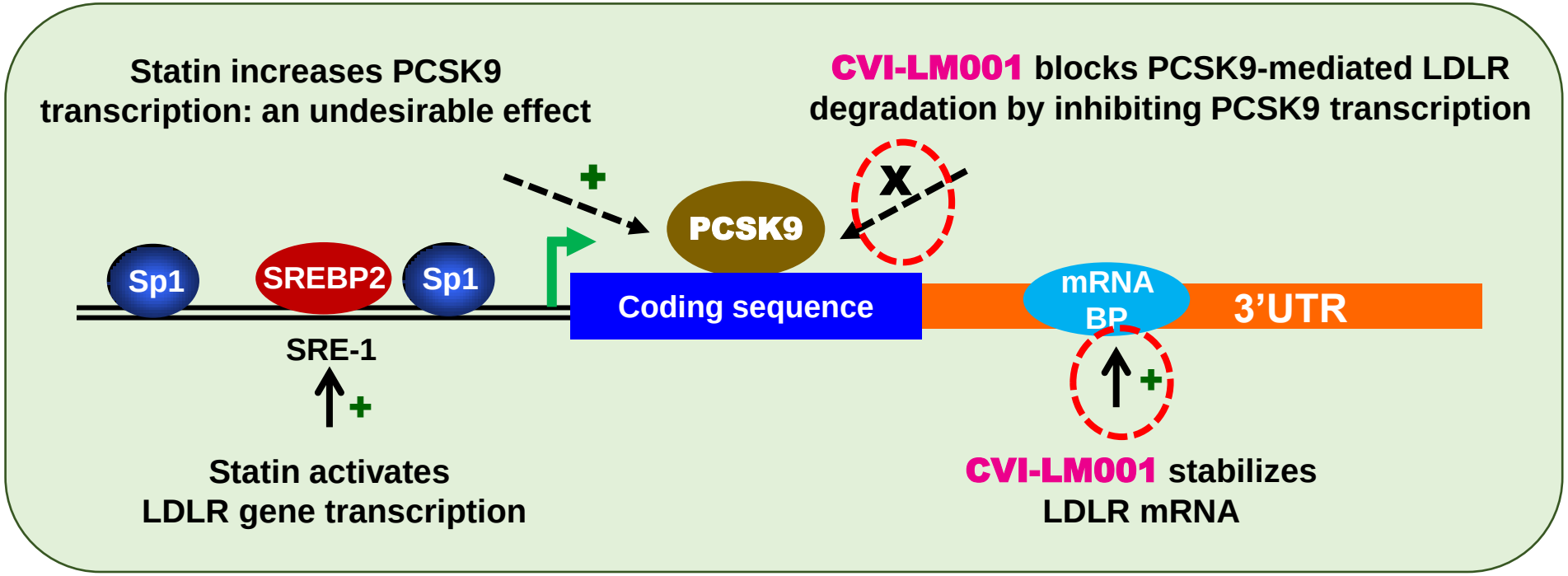
Patients with fatty liver disorders, including NASH and NAFLD, may benefit from reduced liver fat levels. Fatty liver disease is a growing problem globally due to increasing metabolic disorders. Patients with NASH and NAFLD often have associated dyslipidemia. As a result, most NAFLD/NASH patients die from cardiovascular disease.

CVI-LM001 is a novel, first-in-class, safe and oral once daily PCSK9 modulator with distinct mechanisms of action in lowering blood atherogenic LDL-cholesterol and reducing liver fat respectively. Working synergistically with statins, CVI-LM001 has the potential to target patients with hypercholesterolemia and NAFLD/NASH patients with elevated LDL-C. Currently, a 12-week Phase 2 POC trial is initiated in China in patients with hypercholesterolemia.

Pipeline Overview

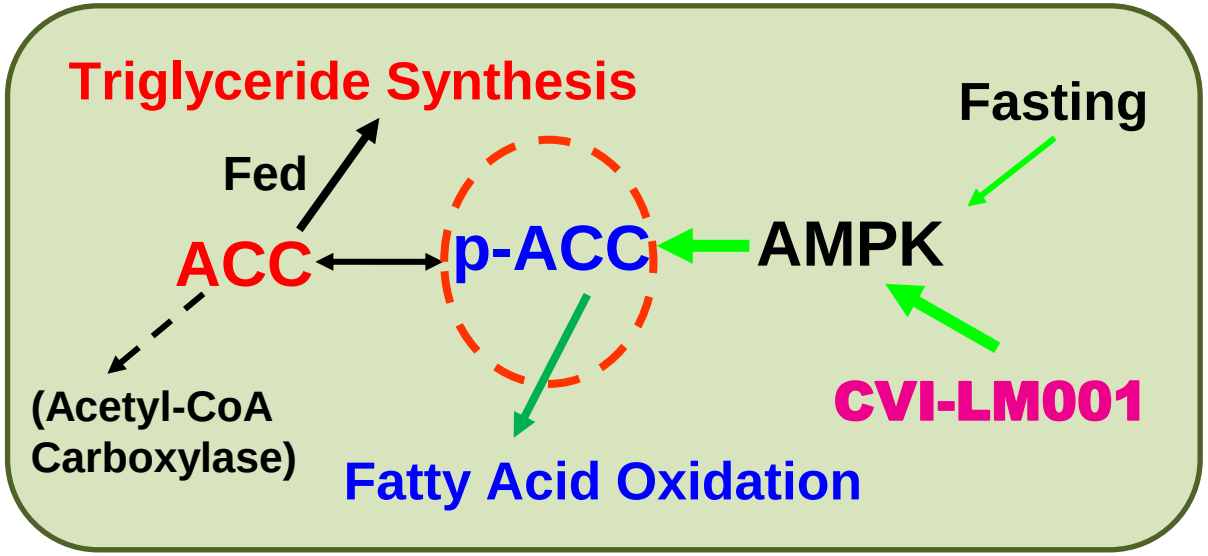


CVI-LM001 Dual Mechanisms of Action to Combat Hyperlipidemia and Fatty Liver Disease



MOA-1: CVI-LM001 upregulates liver LDLR expression and accelerates blood LDL-cholesterol removal via an unique mechanism of inhibition of PCSK9 transcription and prevention of LDLR mRNA degradation; statin activates LDLR transcription via SREBP2 pathway.

LDLR: LDL receptor, SRE-1: sterol-regulatory element, mRNABP: mRNA binding protein, 3'UTR: 3'untranslated region



MOA-2: CVI-LM001 activates hepatic adenosine monophosphate-activated protein kinase (AMPK), a master regulator of cellular energy, which turns on pathways that reduce hepatic fat synthesis and boost fatty acids oxidation.

CVI-LM001 is a novel candidate for cardiometabolic and liver diseases

Preclinical studies:

In a hyperlipidemic hamsters model, treatment with CVI-LM001 (40, 80 and 160 mg/kg, QD) for 4 weeks dose-dependently increased liver LDLR protein levels up to 3.5-fold and decreased circulating PCSK9 levels to 10% of control at the highest dose, this was accompanied by significant reductions in serum LDL-C, TC, and TG. In a diet-induced NASH hamster model, 4 weeks treatment with CVI-LM001 substantially reduced hepatic ballooning and improved NASH score.

Clinical studies:

In a double-blind, randomized Phase 1a study conducted in healthy volunteers, compared to baseline, serum PCSK9 levels was significantly reduced after 10 days of oral treatment with CVI-LM001 (300 mg, QD). Moreover, in a Proof of Mechanism Phase 1b study conducted in subjects with elevated LDL-C, compared with placebo cohort, treatment with CVI-LM001 for 28 days significantly reduced serum LDL-C ,TC , Apo B and PCSK9 levels. CVI-LM001 had a favorable safety profile and was well tolerated in Phase 1 studies conducted in healthy volunteers and hyperlipidemic subjects.

Altogether, these studies demonstrate that CVI-LM001, a novel PCSK9 modulator, has the potential to be a new oral cholesterol-lowering drug and warrant further clinical development. Currently, a 12-week Phase 2 POC trial is ongoing in China in patients with hypercholesterolemia.

CVI-LM002, a novel, oral, best-in-class small molecule targeting obesity, NAFLD/NASH and rare metabolic diseases

CVI Pharmaceuticals has discovered a series of novel small molecules that can significantly improve metabolic disorders in preclinical models. CVI-LM002 is a lead candidate that can induce significant body weight loss and body fat reduction in a diet-induced obese primate model and ameliorate hyperlipidemia and reduce liver fat in HFD-induced hamster models. Based on a number of diverse pharmacologic properties including liver and adipose tissue of this compound, CVI believes that CVI-LM002 can potentially treat patients with obesity and NAFLD/NASH as well as rare metabolic diseases. **CVI-LM002** is currently at pre-IND stage.