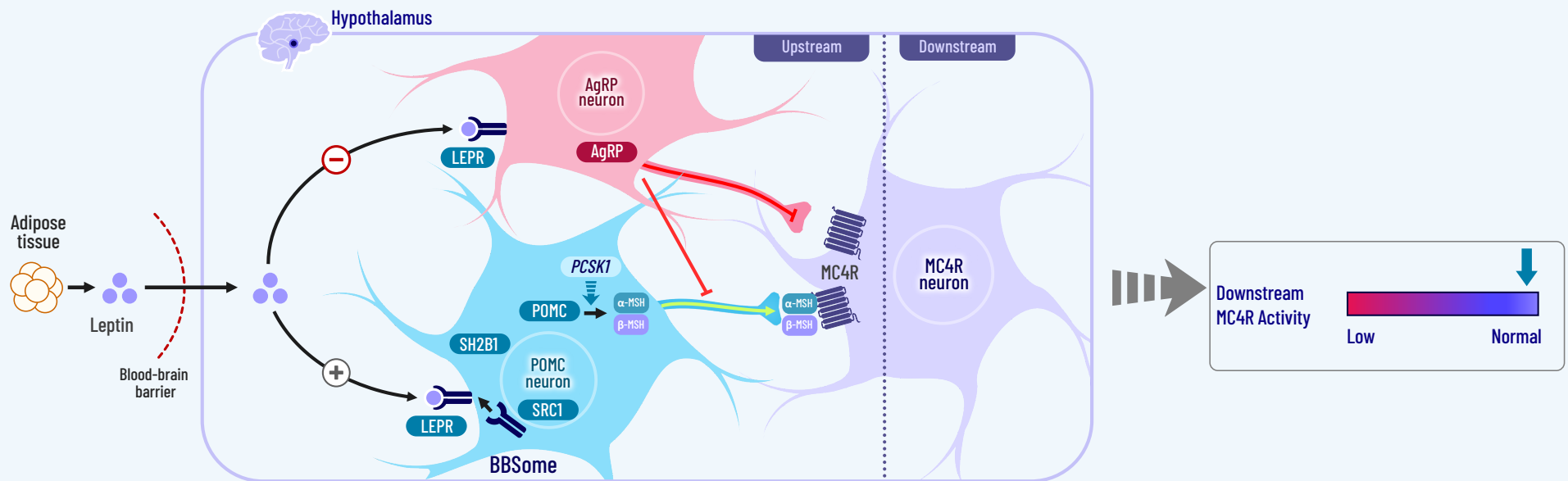


Rhythm Pharmaceuticals is a biopharmaceutical company dedicated to pioneering research and development of treatments for rare melanocortin-4 receptor (MC4R) pathway diseases.

Individuals with rare MC4R pathway diseases are often affected with hyperphagia (pathological, insatiable hunger accompanied by food seeking behaviors) and early-onset, severe obesity.^{1,2}

Body weight is highly regulated. The MC4R pathway regulates hunger, caloric intake, and energy expenditure, consequently affecting body weight.^{1,3-7}

The MC4R Pathway





In some people, genetic variants can impair signaling in the MC4R pathway, leading to hyperphagia and obesity.^{1,3,5}

Abbreviations: AgRP, agouti-related protein; BBSome, complex of 8 Bardet-Biedl syndrome proteins; LEPR, leptin receptor; MC4R, melanocortin-4 receptor; MSH, melanocyte-stimulating hormone; PCSK1, proprotein convertase subtilisin/kexin type 1; POMC, proopiomelanocortin; SH2B1, Src homology 2 B adapter protein 1; SRC1, steroid receptor coactivator 1.

Rhythm Pharmaceuticals is advancing the clinical development program for setmelanotide, an MC4R agonist, as well as investigational MC4R agonists LB54640 and RM-718. In addition, we are working to discover and advance new therapeutic options for patients with congenital hyperinsulinism (CHI).

Rhythm clinical development pipeline

	Patient Population	Pre-clinical	Phase 1/2	Phase 3	Regulatory Approval
Setmelanotide <i>daily formulation</i>	POMC, PCSK1 or LEPR deficiency		US, Canada*		
	Bardet-Biedl syndrome		US, Canada*		
Setmelanotide <i>daily formulation</i>	Hypothalamic obesity		Enrollment complete		
	 Emanate <small>Obesity and Hunger Clinical Trial</small>				
	Pediatrics (age 2 to <6 years, biallelic POMC, PCSK1, or LEPR deficiency or Bardet-Biedl syndrome)				
	 Daybreak <small>Obesity and Hunger Clinical Trial</small>				
Setmelanotide <i>weekly formulation</i>	Switch study with patients previously on setmelanotide				
LB54640	Hypothalamic obesity				
RM-718	Rare MC4R pathway diseases		Ph1 trial 1H2024		
Pre-clinical	Congenital Hyperinsulinism (CHI)	Lead identification underway			

Complete
 Denotes trial underway
 Denotes planned trial

*Other countries include EU, Great Britain, Israel

For more information regarding clinical study opportunities and our ongoing research, please contact clinicaltrials@rhythmtx.com or visit our website at <https://www.rhythmtx.com/>.

Abbreviations: LEPR, leptin receptor; MC4R, melanocortin-4 receptor; PCSK1, proprotein convertase subtilisin/kexin type 1; POMC, proopiomelanocortin.

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Not For Promotion

Rhythm
PHARMACEUTICALS