



# PROHEARINGS

14 OKTOBER, 2021

MEDIVIR

# Today's presenters

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Chief Financial Officer



Magnus Christensen

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# Executive summary

# Executive summary

## Proprietary clinical asset MIV-818

- MIV-818 – A liver directed nucleotide prodrug
- MIV-818 has received Orphan drug designation (ODD) by EMA and FDA for the treatment of hepatocellular carcinoma (HCC)
- Phase 1b/2a – upcoming combination study

## Other clinical programs

- IGM Biosciences - exclusive licensing agreement for birinapant
- Remetinostat and MIV-711 for partnering/out-licensing

Founded: 1988

Listed: Nasdaq OMX

Location: Stockholm

Cash position: SEK 248M<sup>1)</sup>

Market Cap: SEK 530M<sup>2)</sup>

FTE: 9



1) Q2 report

2) 2021-10-12






## Focused clinical program

Nucleotide prodrug	Indication	Preclinical	Phase I	Phase II	Exclusivity
MIV-818	Liver cancer				IP : 2035

## Partnered assets in clinical development

Compound	Mechanism	Indication	Phase I	Phase II	Partner	Exclusivity
Birinapant (IGM-9427)	SMAC mimetic	Solid tumors				IP : 2034

## Multiple clinical programs for partnering/out-licensing

Compound	Mechanism	Indication	Phase I	Phase II	Phase III	Exclusivity
Remetinostat	Topical HDAC	MF-CTCL <sup>1)</sup> BCC				IP : 2034
						
MIV-711	Cathepsin K inhibitor	Osteoarthritis				IP : 2034

1) Indications: basal cell carcinoma, squamous cell carcinoma, mycosis fungoides cutaneous T-cell lymphoma (phase III ready)

# Analysts covering Medivir

Richard Ramanius, Redeye

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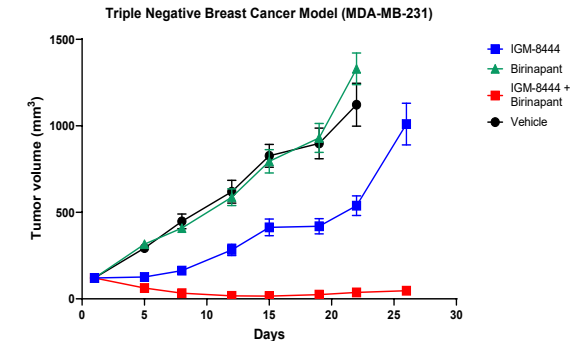
# Partnerships

# Delivering on our partnering strategy

Asset	Date	Partner(s)	Type of deal	Potential future revenues
Xerclear	Feb 2020	SYB	Out-licensing	Royalties
Undisclosed target	Feb 2020	Undisclosed biotech	Option	Option fee
USP-1	March 2020	Tango Therapeutics	Out-licensing	Milestones and royalties
Birinapant	Dec 2020	Tetralogic	Re-negotiated to enable an outlicensing deal	
Birinapant	Jan 2021	IGM Bioscience	Out-licensing	Milestones and royalties
USP-7	Feb 2021	Ubiquigent		Revenue share
Remetinostat	August 2021	Several stakeholders	Re-negotiated to enable an outlicensing deal	

# Birinapant - Licensing agreement with IGM Biosciences

- IGM is a clinical-stage biotechnology company focused on creating and developing engineered IgM antibodies
- Birinapant is initially intended to be combined with IGM-8444, an IgM antibody targeting Death Receptor 5 (DR5) being developed by IGM, and birinapant has been shown to enhance anti-tumor activity preclinically.
- Clinical testing of birinapant (IGM-9427) in combination with IGM-8444 expected to begin this year<sup>1</sup>
- Should birinapant be successfully developed and approved, Medivir is entitled to receive development, regulatory and sales milestone payments up to a total of approximately USD 350 million plus tiered royalties from the mid-single digits up to mid-teens on net sales



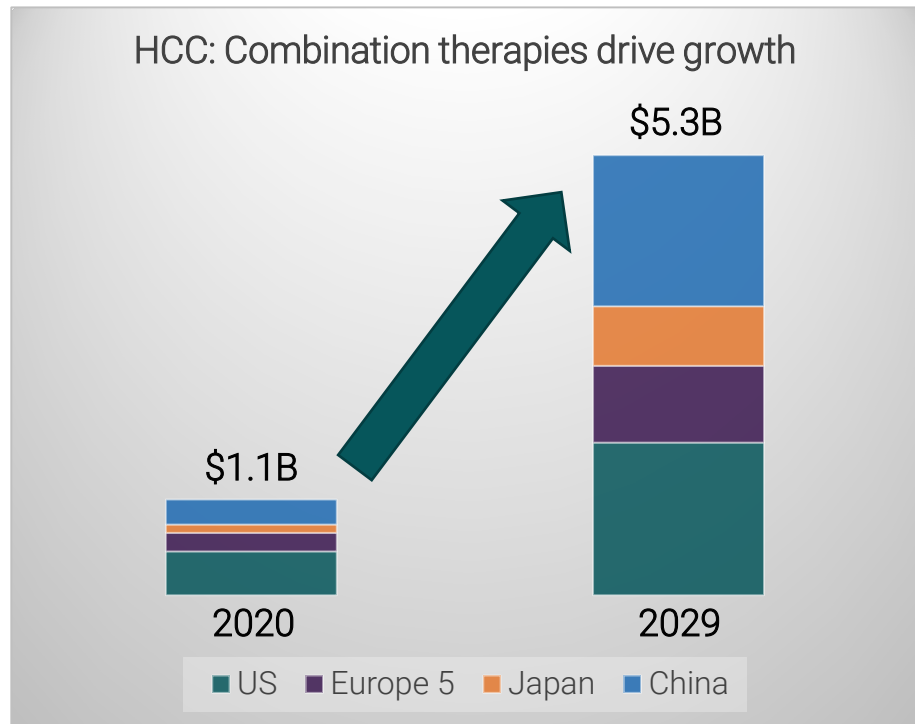
Open-label, Multicenter, Phase I Study with IGM-8444 in combination with Birinapant (IGM-9427) in patients with solid tumors will be in two stages: a dose-escalation stage and an expansion stage (NCT04553692)

<sup>1</sup>IGM Biosciences Q2 Report



**MIV-818** — *for the treatment of liver cancer*

# Hepatocellular carcinoma (HCC) is a growing market



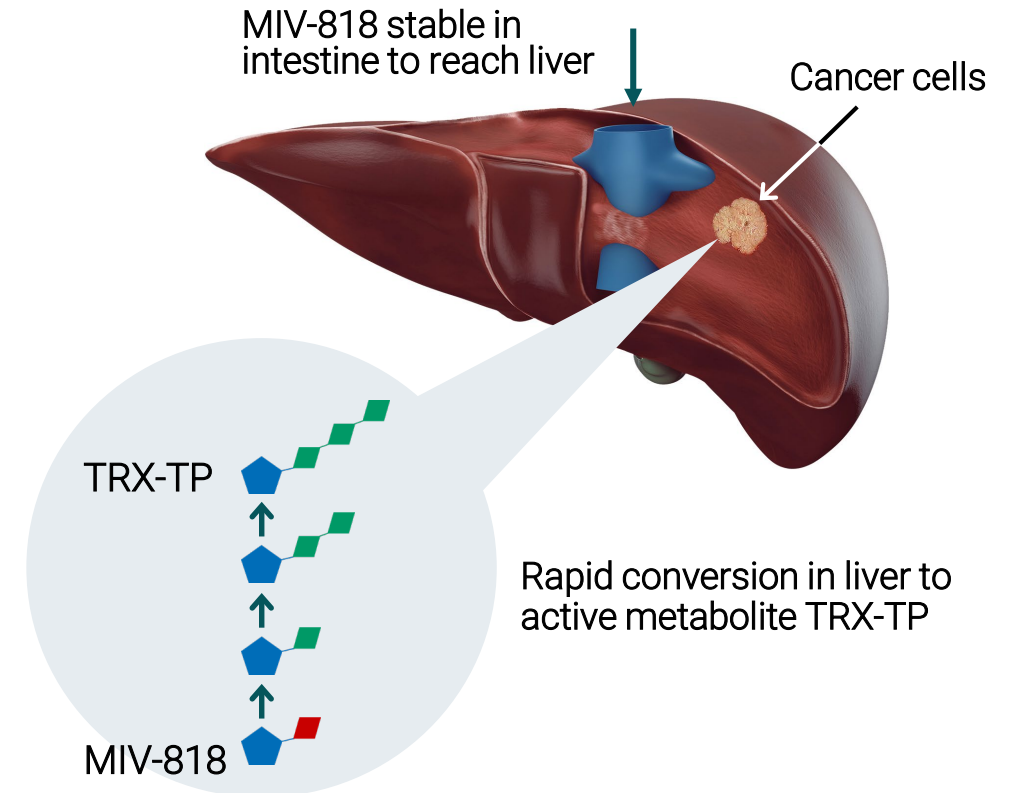
Source: GlobalData 2021

- Continued very high unmet medical need in HCC
  - Despite recent advances in treatment of HCC, there is still a large group of patients that do not respond to or are intolerant to current treatments
- The HCC market growth is driven by;
  - Combination therapies (especially immuno-oncology combinations)
  - More patients receiving therapy when patients are treated in earlier disease stages
- Liver cancer incidence and mortality are increasing and 5-year survival for those with advanced disease is less than 3% (<https://seer.cancer.gov/statfacts/html/livibd.htm>)



# MIV-818 – Introduction

- Novel nucleotide prodrug inhibiting DNA-replication of tumor cells, targeting cancer cells in the liver
- Orphan Drug Designation has been granted in HCC by the FDA and EMA



Designed to deliver high levels of active metabolite, troxacitabine-triphosphate (TRX-TP) to the liver while minimizing systemic exposure

# MIV-818 – Study design phase 1 monotherapy

## Population studied

- advanced inoperable HCC, intrahepatic bile duct cancer and liver metastatic disease from solid tumors
- 9 patients (Phase 1a) doses of 3-70 mg for 3-5 days in 21-day cycles, 10 patients (Phase 1b) dose escalation starting at 40 mg for 5 days in 21-day cycles
- adult patients that had exhausted all approved therapies

## Primary objective

- to assess safety and tolerability of MIV-818 as monotherapy
- to determine the recommended phase 2 dose for monotherapy

## Secondary objective

- to evaluate tumor response rate based on RECIST v1.1

## Exploratory objective

- to assess pharmacokinetics and pharmacodynamic effects of MIV-818

# MIV-818 - Safety summary

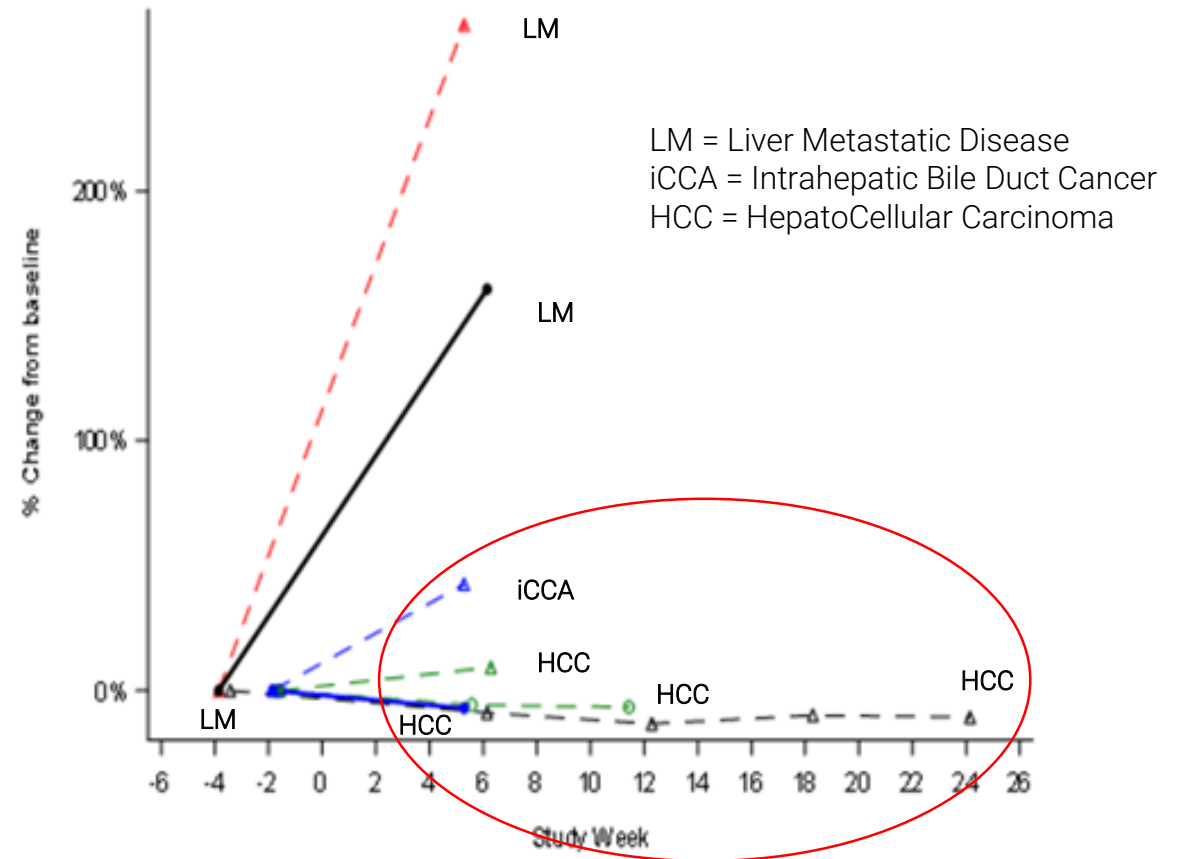
- Overall safety and tolerability profile in line with expectations for this type of advanced cancer patients
  - Decreases in blood counts were seen frequently with MIV-818 but resolved rapidly and are easily monitored
- Supports evaluating MIV-818 in combination with other drugs in next phase of development

# Summary of efficacy phase 1b

- Four HCC patients showed stable disease in the liver over an extended period of time
- Based on objective response (RECIST v1.1) data, 4/7 primary liver cancers (HCC, iCCA) had stable disease as best overall response
- One HCC patient remained on treatment for 8 months

Supports our decision to study HCC in upcoming combination study

Phase 1b change in liver target lesions\*

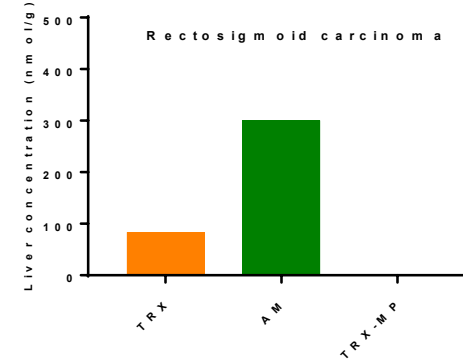


\*Out of 10 enrolled patients, one did not complete safety follow up and one lacked independent radiologist assessment

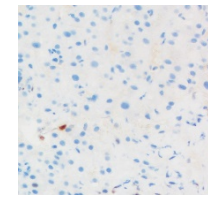
# MIV-818 POC demonstrated by liver biopsies

- Evidence of MIV-818 delivery to the tumor (measured MIV-818 metabolites)
- Clear signs of MIV-818 induced DNA-damage in tumor tissue
- MIV-818 induced effect observed across different types of liver cancer
- No observable effects in normal liver tissue

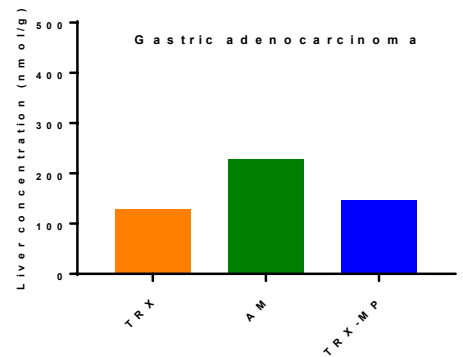
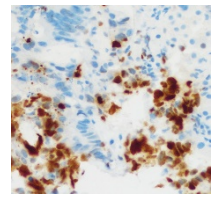
Biopsies from two MIV-818 treated patients



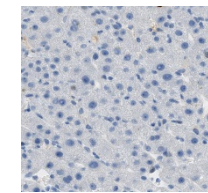
Normal liver



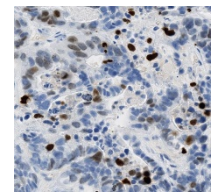
Tumor



Normal liver



Tumor



PD marker  $\gamma$ H2AX (% positive cells/brown stain) shows MIV-818 induced DNA-damage in tumor cells and not normal liver tissue



# Conclusions MIV-818 phase 1 monotherapy

- Safety profile to date supports moving forward with development. Decreases in blood cell counts were the most common side effects, these resolved quickly
- In Phase 1b four patients out of seven with primary liver cancer (e.g. HCC, iCCA) had stable disease as best overall response; one stayed on treatment for eight months
- Liver biopsy data has demonstrated delivery of MIV-818 to the liver, and a selective effect of MIV-818 on cancer cells vs normal liver tissue, across different types of cancer

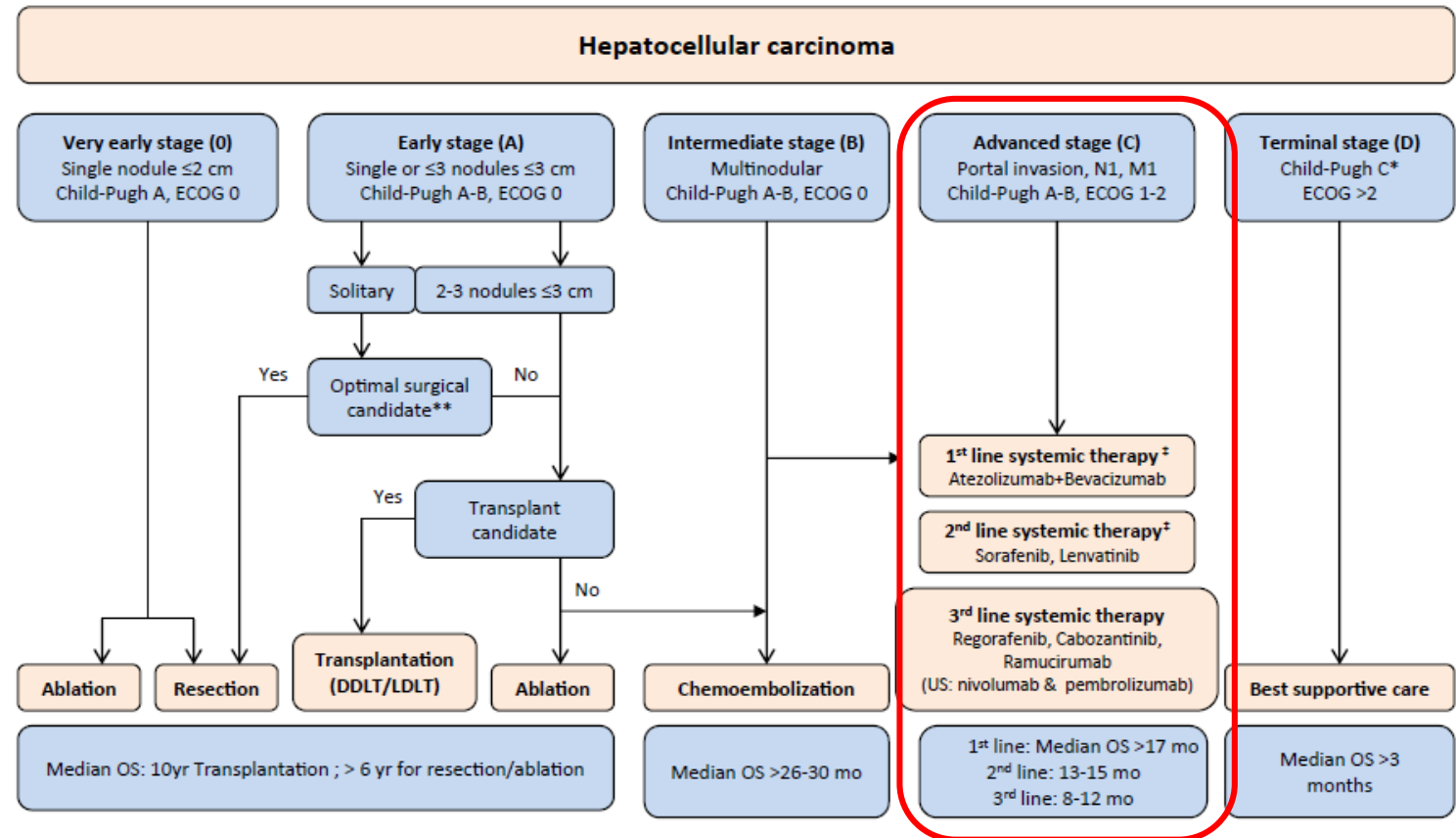
The clinical data from phase 1a and 1b monotherapy, supports continued development of MIV-818

# The treatment landscape of advanced HCC

# HCC Epidemiology and current treatments

Primary liver cancers: 850,000 cases worldwide annually

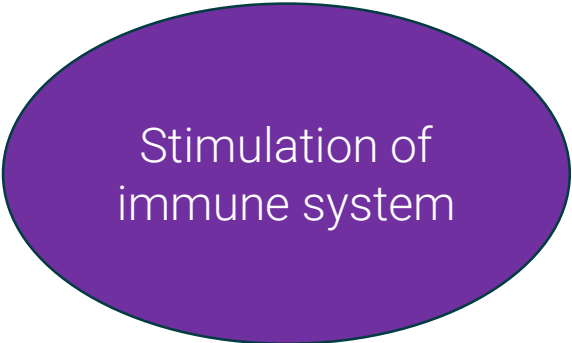
- 90% are hepatocellular carcinoma (HCC)
- 3rd leading cause of cancer-related death, with 600,000 deaths worldwide



Llovet et al Hepatology vol 73, 2021

# MIV-818 – A new unique tool in HCC

Current development pipeline of new HCC-therapies consists of a variation of combination trials with two main mechanisms of actions



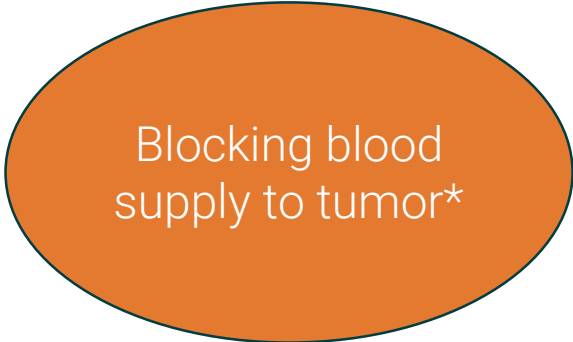
Stimulation of  
immune system

*Marketed drugs (anti-PD1):*

Keytruda®

Opdivo®

Tecentriq®



Blocking blood  
supply to tumor\*

*Marketed drugs:*

Lenvima® (Tyrosine Kinase)

Nexavar® (Tyrosine Kinase)

Avastin® (anti-Vascular Endothelial Growth Factor)

\* Some of these drugs are multifunctional and have additional functions

# MIV-818 – to be explored in combinations in HCC

Inhibition of DNA replication

- represents a unique mechanism to treat HCC selectively targeting tumor cells in the liver
- adds a novel tool that may be combined with or added to any of the two main mechanisms

*Our upcoming trial will study MIV-818 with each of these mechanisms:*

Stimulation of immune system

MIV-818 +

Keytruda®

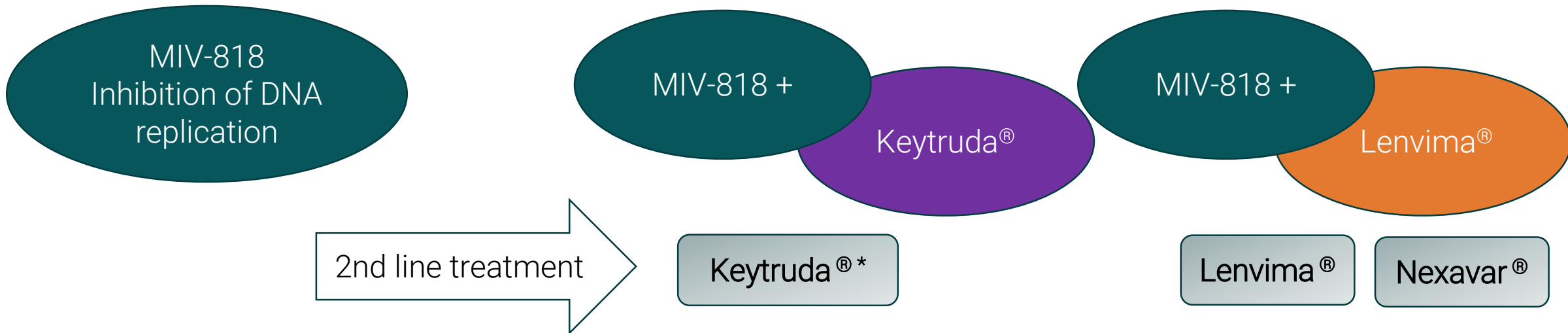
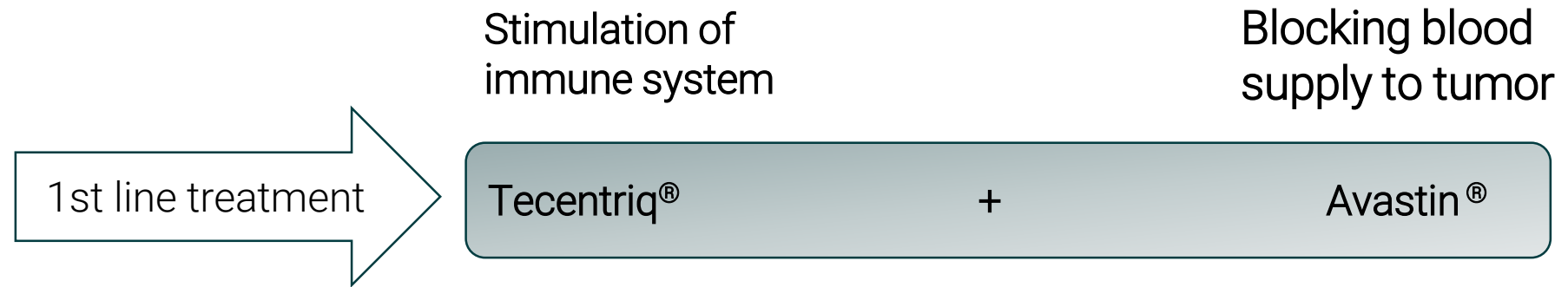
Blocking blood supply to tumor

MIV-818 +

Lenvima®



# MIV-818 - aiming to be the new improved second line treatment



\* Keytruda® only approved as monotherapy in HCC in US

# Next step in our development of MIV-818

# MIV-818 combinations enhances efficacy in tumor models



Keytruda®

- Combination of MIV-818 and Keytruda® results in stronger inhibition of tumor growth than either drug alone
- Signs of enhanced immune activity in tumors observed

## Scientific rationale:

- MIV-818 induces DNA damage and tumor cell death, potentially leading to increased tumor antigen presentation and increased immune response



Lenvima®

- Addition of MIV-818 to Lenvima® in a preclinical model significantly enhances efficacy

## Scientific rationale:

- TKIs inhibit angiogenesis and induce tumor hypoxia
- Hypoxia increases the expression of the enzyme (PGK1) that generates active MIV-818, resulting in higher levels of active metabolite in the tumor

# Phase 1b and phase 2a combination study

## Patient population to be studied

- advanced inoperable HCC
- must have progressed on or are intolerant of first line standard therapy for HCC and are candidates for Keytruda<sup>®</sup> or Lenvima<sup>®</sup> treatment

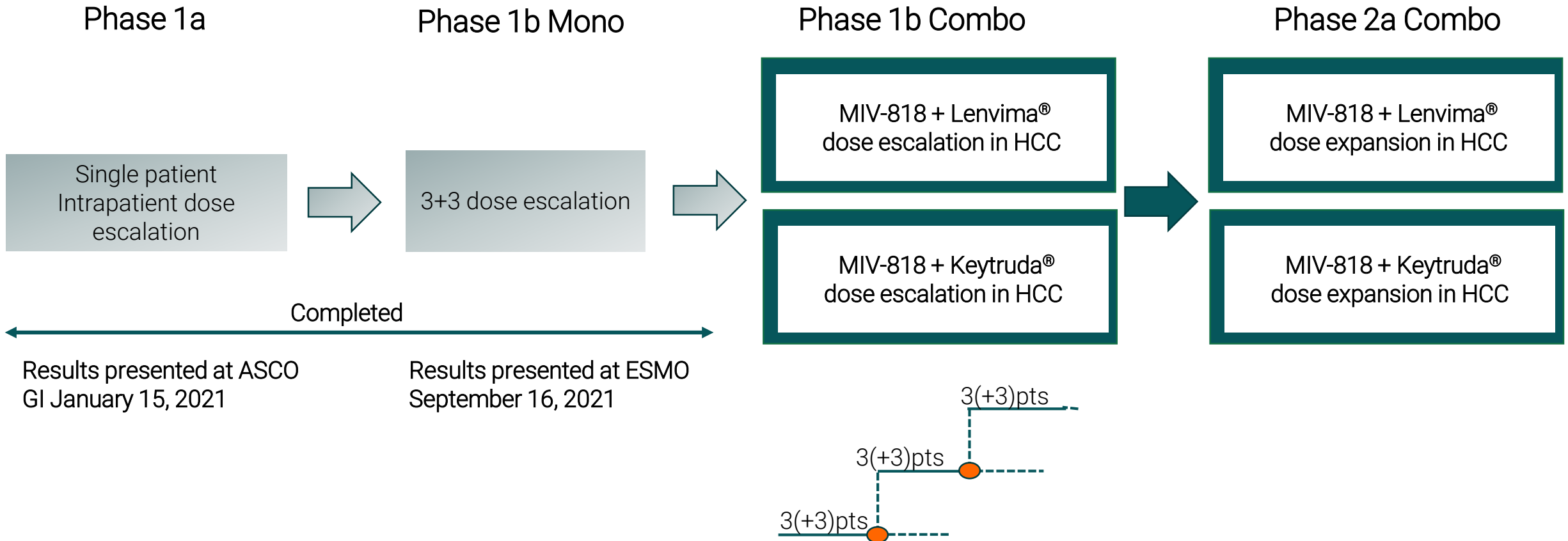
## Primary objective

- to assess safety and tolerability of MIV-818 in combination with Keytruda<sup>®</sup> or Lenvima<sup>®</sup>
- to determine recommended phase 2 dose for MIV-818 in combination with Keytruda<sup>®</sup> or Lenvima<sup>®</sup>

## Secondary objective

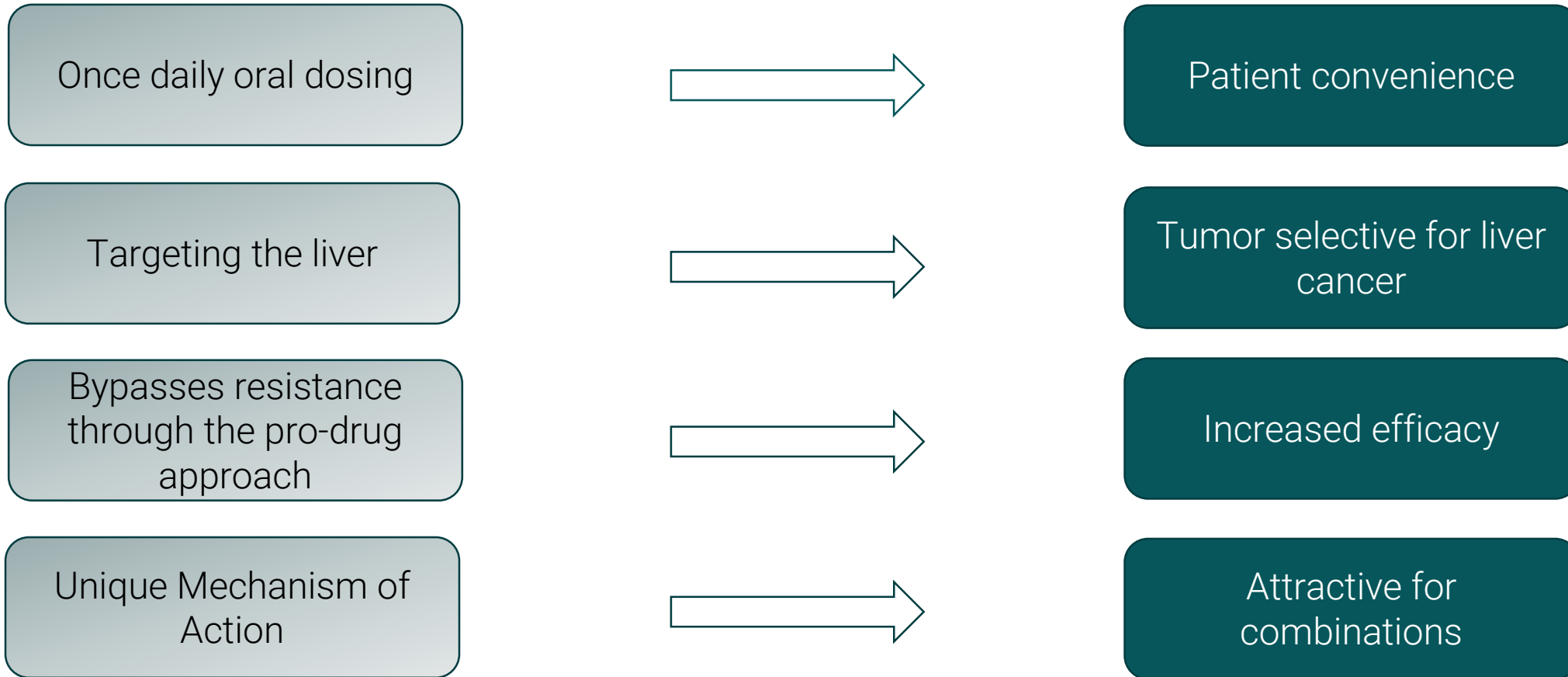
- to evaluate tumor response rate based on RECIST v1.1

# Upcoming combination study in 2nd line HCC





# MIV-818 – Key advantages



# On track to initiate the combination study in 2021 as planned

- The clinical combination study with MIV-818 has been approved in UK, where additional sites will be opened
- We also plan to open sites in Spain and South Korea
- The sites in South Korea will be beneficial from patient recruitment perspective as HCC is much more common in Asia
- Asia is an important future market and exposure in Asian population will aid in finding potential future partners

# Upcoming milestones 2021

# Upcoming milestones 2021

MIV-818: First patient in combination study expected to be enrolled	Q4 2021
Birinapant: IGM plan to start a combination study with birinapant (IGM-9427) and IGM-8444	Q4 2021



**Thank you!**