



# ERIK PENSER BANK

FEBRUARY 24, 2022

MEDIVIR

# Today's presenter



**CEO**

- Jens Lindberg
  - Joined Medivir 2022
  - > 25 years pharma experience with focus in Oncology.
  - Has led global product strategy development for late-stage compounds as well as product launch for multiple compounds.
  - Experience includes interim CEO role for Sedana Medical AB.
- 
- Medivir ownership; 0 shares & 240.000 warrants

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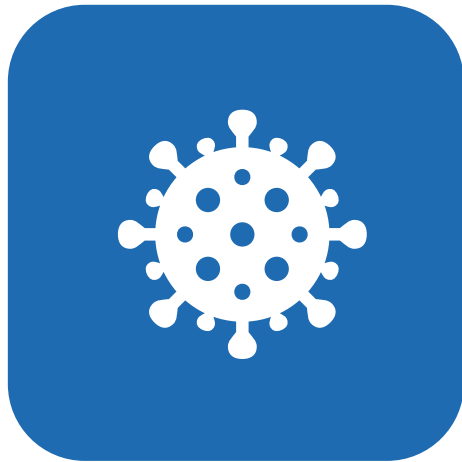
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# Medivir – transformation journey well underway



**Focused strategy with clear priority & momentum for exciting lead asset**



**Experienced & engaged management team & board**



**Remaining assets either out-licensed or re-negotiated to enable valued adding deals**

# Medivir – a company with a clear mission & key priorities

Improving life for cancer patients through transformative drugs

1

Accelerate  
product development  
for lead asset MIV-818  
/fostroxacitibine  
bralpamide

2

Maximise value of  
assets for partnering  
& out-licensing

3

Inspiring  
place to work &  
an entrepreneurial  
company culture

# Significant progress in 2021 delivering on key strategic priorities

## Key progress made in 2021

### Accelerating fostroxacitabine bralpamide

- Phase 1b monotherapy data presented supporting continued development
- Decision to continue development as combination therapy & phase 1b/2a combo study initiated with Keytruda® or Lenvima®
- MIV-818 awarded INN fostroxacitabine bralpamide, highlighting its unique MoA

### Maximise value of assets for partnering & out-licensing

- Initiation of clinical study with birinapant + IGM-8444 (DR5) in patients with solid tumors
- Re-negotiated deal for remetinostat improving Business Development potential
- Remetinostat data published in both BCC & SCC, further supporting BD potential



# MIV-818/fostroxacitabine bralpamide

– *for the treatment of liver cancer*



# Three focus areas in pharmaceutical drug development



Commercial potential &  
unmet need



Differentiation /  
uniqueness



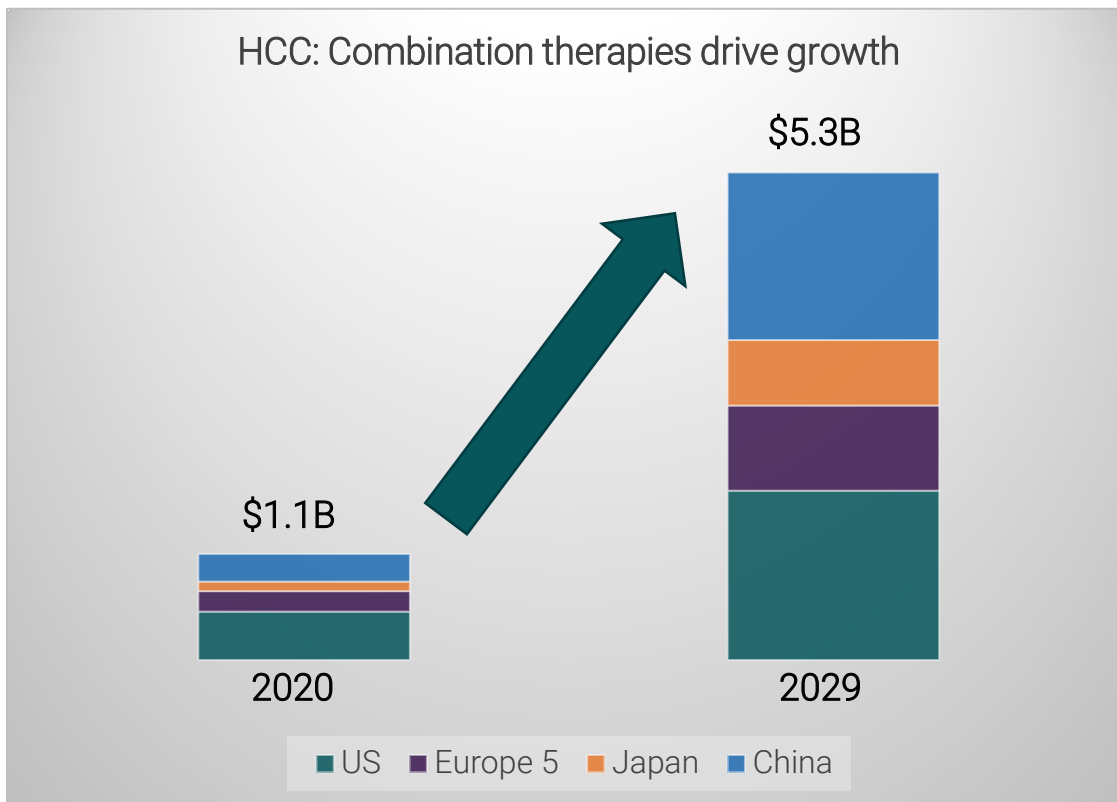
Technical risk  
minimisation



# HCC is a significantly growing market with large unmet need

HCC market estimated to grow almost five-fold until 2029

Despite recent advancements, unmet need is still high



- Liver cancer incidence and mortality are increasing and 5-year survival for those with advanced disease is less than 3%<sup>1</sup>
- Liver cancer is the third leading cause of cancer death worldwide<sup>2</sup>
- 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 and patients treated in earlier disease stages

Source: GlobalData 2021

<sup>1</sup>(<https://seer.cancer.gov/statfacts/html/livibd.htm>)

<sup>2</sup> Sayiner M, et al. Digestive Diseases and Sciences. 2019; 64: 910-917



# Large unmet need remains despite recent advances in HCC

## 1L – Combinations with some incremental improvements

Study (phase)	HIMALAYA (III)	IMbrave150 (III)	REFLECT (III)	SHARP (III)
Drug	Imfinzi/ tremelimumab	Tecentriq/ Avastin	Lenvima	Nexavar
Current status	Phase III	Approved 2020	Approved 2018	Approved 2007
Control	Nexavar	Nexavar	Nexavar	Placebo
MoA	anti PDL1/ anti CTLA4	anti PDL1/ anti VEGF	MKI	MKI
mOS (months)	16.4	19.2	13.6	10.7
PFS (months)	NA	6.8	7.3	5.5
ORR	20%	28-33%	19-41%	NA
Company	AZ	Roche	Eisai	Bayer

## 2L – Similar development confirming benefit of combos

Study (phase)	KEYNOTE-224/394 (II/III) <sup>2</sup>	RESOURCE (III)	CHECKMATE-040 /459 (I/II) <sup>1</sup>	CHECKMATE-040 Cohort 4 (I/II) <sup>1</sup>
Drug	Keytruda	Stivarga	Opdivo	Opdivo/ Yervoy
Current status	Accelerated approval 2018	Approved 2017	Accelerated approval (withdrawn)	Accelerated approval 2020
Control	NA	Placebo	Nexavar	NA
MoA	Anti PD1	MKI	anti PD1	anti PD1/ anti CTLA4
mOS (months)	NA/14.6	10.6	NA/16.39	NA
PFS (months)	NA/2.6	3.1-3.4	NA	NA
ORR	17%/13%	11%	14%/15%	33-35%
Company	Merck&Co	Bayer	BMS	BMS

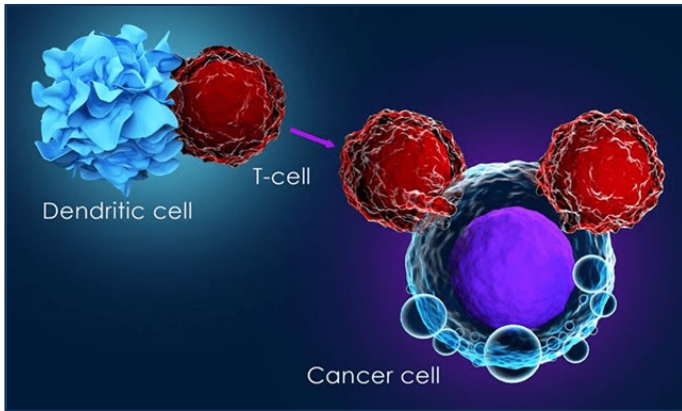
<sup>1</sup> Ongoing phase III study for first line therapy, CheckMate 9DW

<sup>2</sup> Several ongoing phase III studies in different settings and in combination with Lenvima Slide 11

Sources: FDA, BIOMEDTRACKER

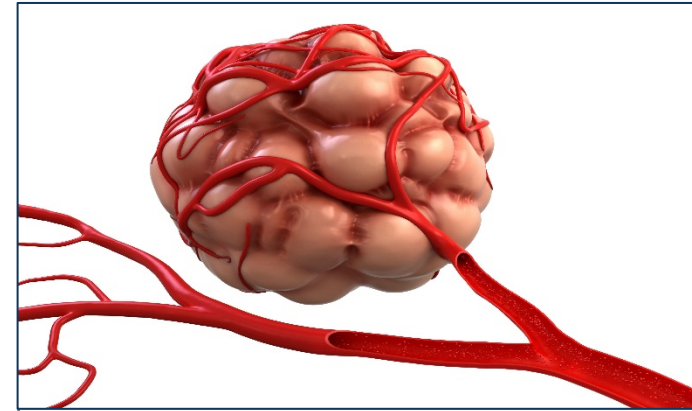
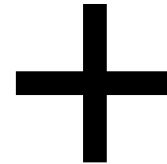


# Current pipeline of new HCC therapies consists of a variation of combination trials with two key mechanisms of actions



## Stimulation of immune system

- Keytruda (PD-1)
- Tezentriq (PD-L1)
- Opdivo (PD-1)
- Imfinzi (PD-L1)
- Yervoy (CTLA-4)
- Tremelimumab (CTLA-4)



## Blocking blood supply to tumor\*

- Avastin
- Nexavar
- Lenvima
- Stivarga
- Cometriq/Cabometyx

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

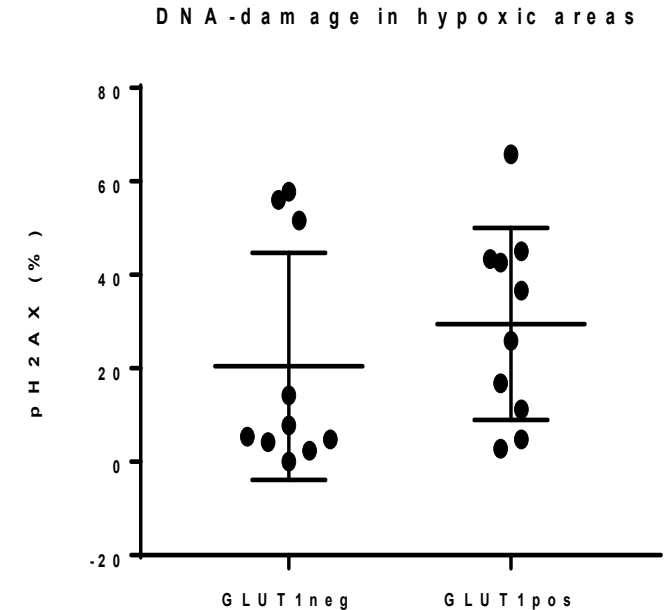
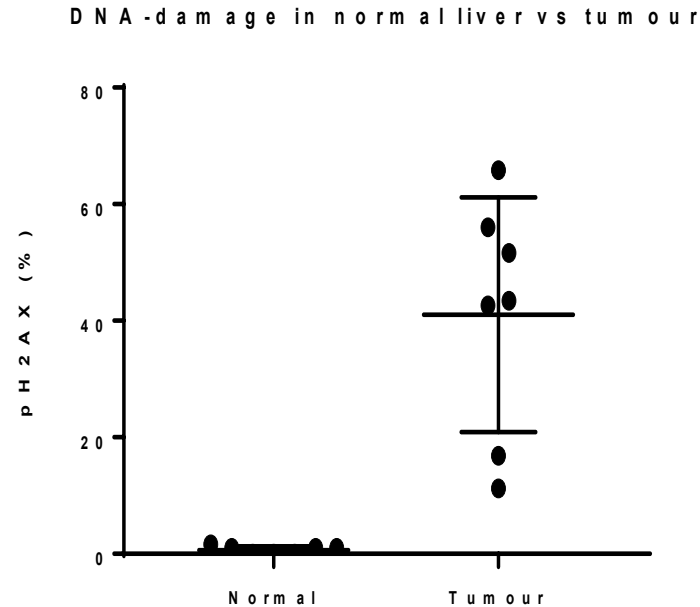
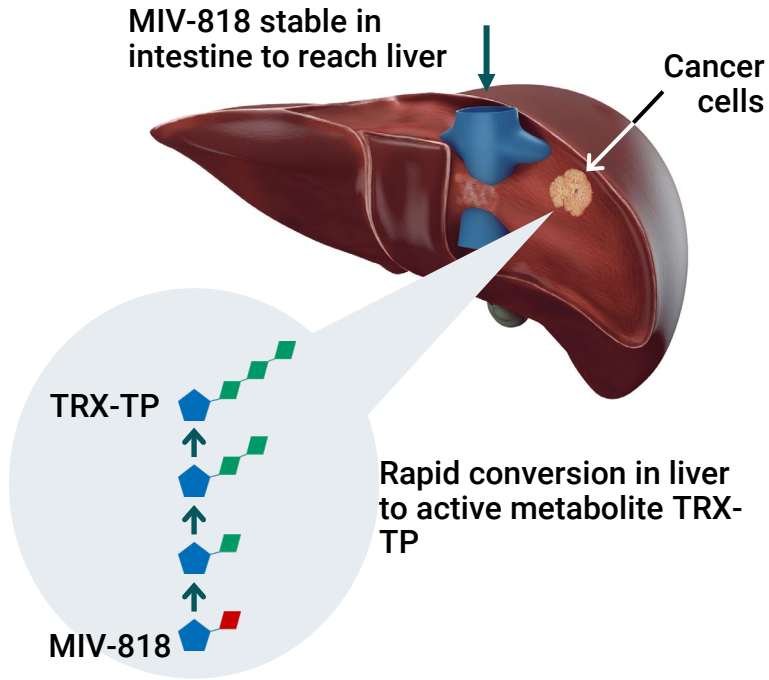


# Differentiated mechanism – induces DNA damage & cell death selectively in tumor tissue in the liver

Designed to reach the liver & minimise systemic exposure

DNA-damage observed in tumor tissue but not in normal liver tissue\*

Ability to induce DNA-damage in difficult to treat regions in cancer\*



\*PD marker gH2AX (% positive cells/brown stain) shows MIV-818 induced DNA-damage in tumor cells and not normal liver tissue



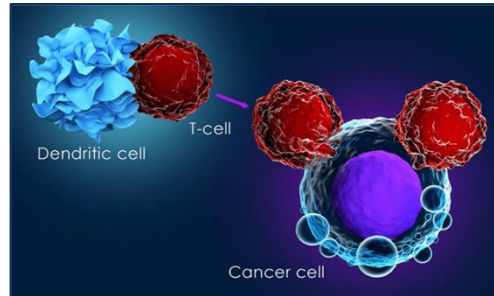


# A new, unique tool in HCC inhibiting DNA replication with strong potential for combinations

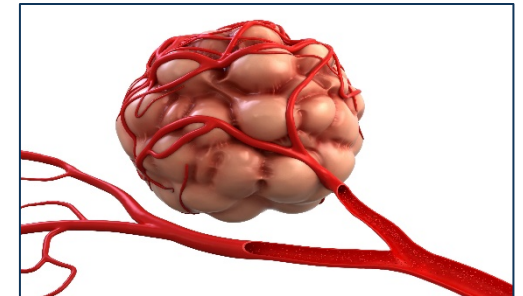
MIV-818 + stimulation of immune system (PD-1)

MIV-818 + blocking blood supply to tumor (TKI)

MIV-818 /  
fostroxacitabine  
bralpamide



MIV-818 /  
fostroxacitabine  
bralpamide



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

“TKI’s induce lack of oxygen in tumours leading to increased PGK1\* expression and most importantly higher levels of MIV-818 active metabolite”

\*Phosphoglycerate kinase 1 – hypoxia inducible gene



# MIV-818 = fostroxacitabine bralpamide

No need for 1<sup>st</sup> phosphorylation providing increased potency & avoidance of resistance mechanisms with potential for a more optimal dose

The mechanism of action, inhibition of cancer cells DNA-replication and induction of DNA-damage & cell death is well established in cancer therapy

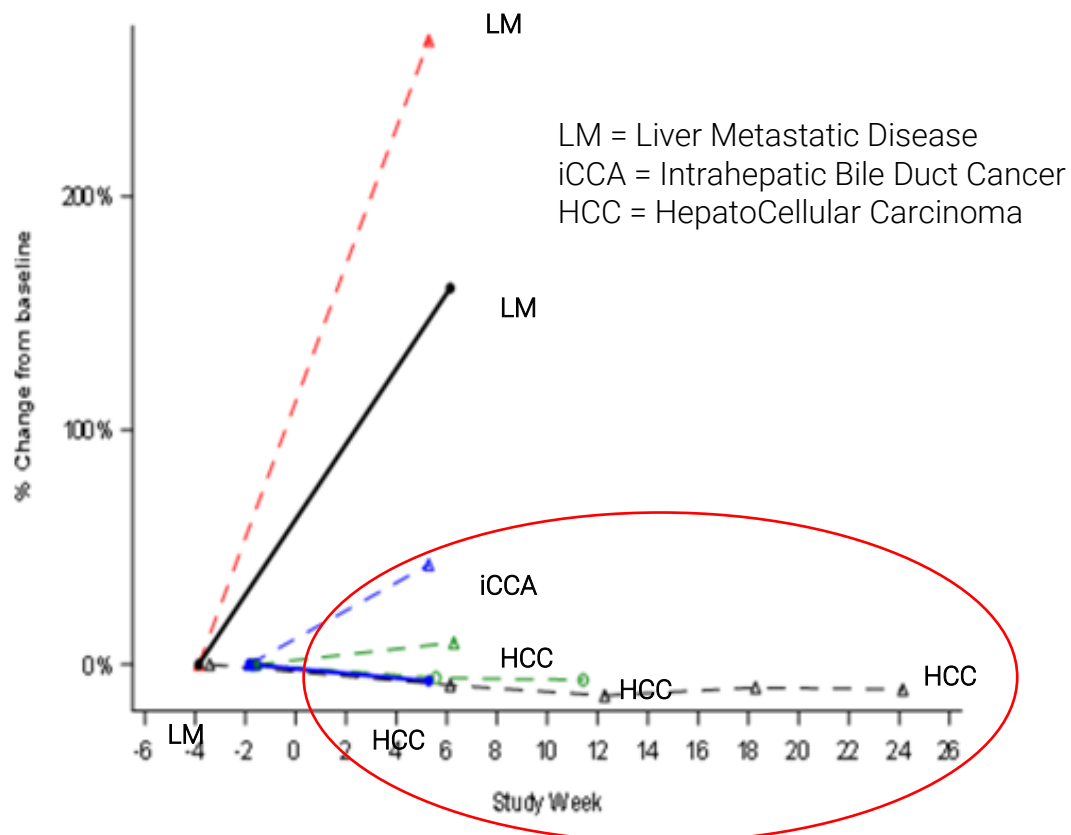
This type of pro drug has already successfully proven its targeted, clinical efficacy in the liver within anti-HCV treatment

Tried & tested mechanism of action minimizing technical risk



# Phase 1b monotherapy results presented at ESMO supports continued development of fostroxacitabine bralpamide

Encouraging changes in liver target lesions\*



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

Safety profile 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

# Fostroxacitabine bralpamide – Key differentiating benefits

**Improved probability  
of success**



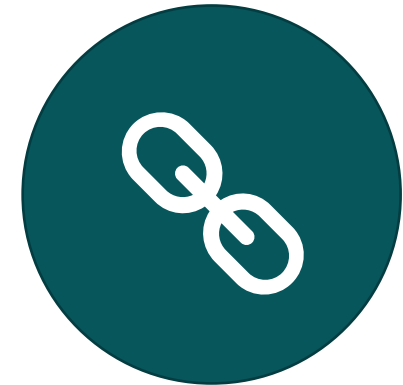
Induction of DNA-damage & cell death already well established in cancer, confirmed by phase 1 data

**Maximum clinical efficacy,  
minimised systemic exposure**



Tumor selective efficacy in the liver that bypasses resistance mechanisms

**Potential for  
synergistic combinations**



Unique mode of action in primary liver cancer



**MIV-818/fostroxacinibine bralpamide**  
– *next step; phase 1b/2a combination study*





# Ongoing phase 1b/2a combination study in 2nd line HCC exploring combinations with both anti-PD-1 & TKI

Dose escalation – phase 1b

Dose expansion – phase 2a

Study Details & Objectives

## Decision point

- Finalise phase 2 dose for each combination
- Which combination(s) to take into phase 2, one or both

### MIV-818 + Lenvima®

10-40 mg, dose cohorts of 3 patients

### MIV-818 + Lenvima®

Recommended Ph 2 dose, n=15/30\*

### MIV-818 + Keytruda®

10-40 mg, dose cohorts of 3 patients

### MIV-818 + Keytruda®

Recommended Ph 2 dose, n=15/30\*

Investigator sites split 60/40 EU & Asia

Patient Population:

- 2L advanced inoperable HCC, Child-Pugh A & B
- progressed on or intolerant of 1L SOC therapy for HCC, including atezo/bev patients

Primary Objective:

- assess safety and tolerability as combination therapy
- determine recommended phase 2 doses

Secondary Objective:

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

\*15 patients per arm if both arms are taken forward or potentially 30 if one combination is chosen

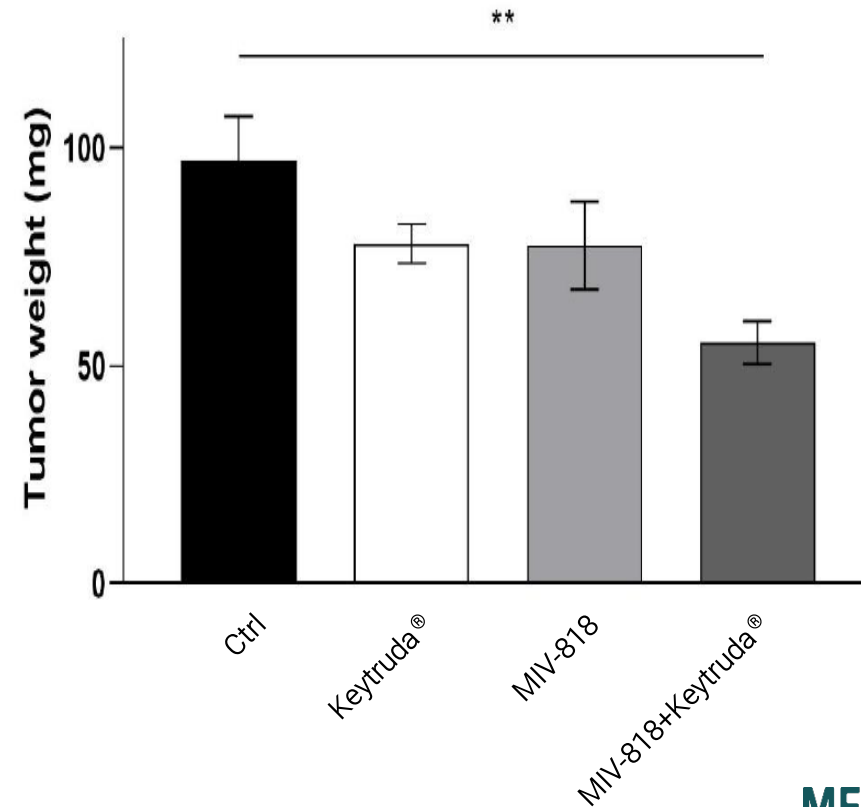


# Combination with Keytruda<sup>®</sup> enhances efficacy in tumor models

Strong rationale supporting MIV-818 + immunotherapy

- MIV-818 induces DNA damage and tumor cell death, potentially leading to increased tumor antigen presentation and increased immune response
- Single agent aPD-1 therapy have shown limited efficacy in HCC
- Combination of MIV-818 and Keytruda<sup>®</sup> results in stronger inhibition of tumor growth than either drug alone
- Signs of enhanced immune activity in tumors observed

MIV-818 + Keytruda<sup>®</sup> tumor model supporting synergy\*



\*MIV-818 plus Pembrolizumab anti-tumour efficacy in vivo, in the chicken chorioallantoic membrane (CAM) H460 tumour model. Tumour growth was assessed by excision and weighing of the tumour at day 18, after treatment with MIV-818 (5uM, day E10-E14) and Pembrolizumab (2mg/kg, day E10-E17).

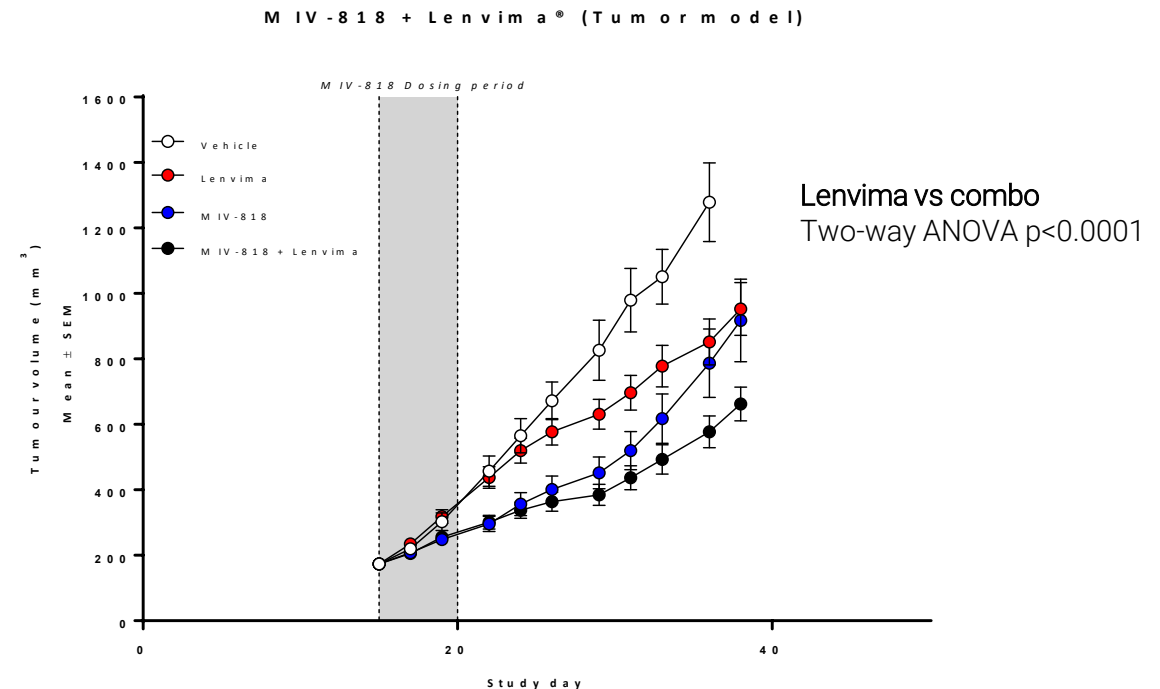


# Combination with Lenvima<sup>®</sup> enhances efficacy in tumor models

Strong rationale supporting MIV-818 + TKI's

- The enzyme PKG1 mediates the last step in generating the MIV-818 active metabolite. PKG1 expression is increased by lack of oxygen, leading to higher levels of active metabolite
- Tyrosine kinase inhibitors such as Lenvima<sup>®</sup> induce lack of oxygen in tumors
- Addition of MIV-818 to Lenvima<sup>®</sup> in a preclinical model significantly enhances tumor growth inhibition

MIV-818 + Lenvima<sup>®</sup> tumor model supporting synergy\*



Dosing:

- MIV-818 30mg/kg BID 5 days
- Lenvima 3mg/kg QD 21 days

\*Anti-tumour efficacy of MIV-818 (30mg/kg BID 5 day plus Lenvatinib (3mg/kg QD 21 days) in the HepG2 mouse HCC model.

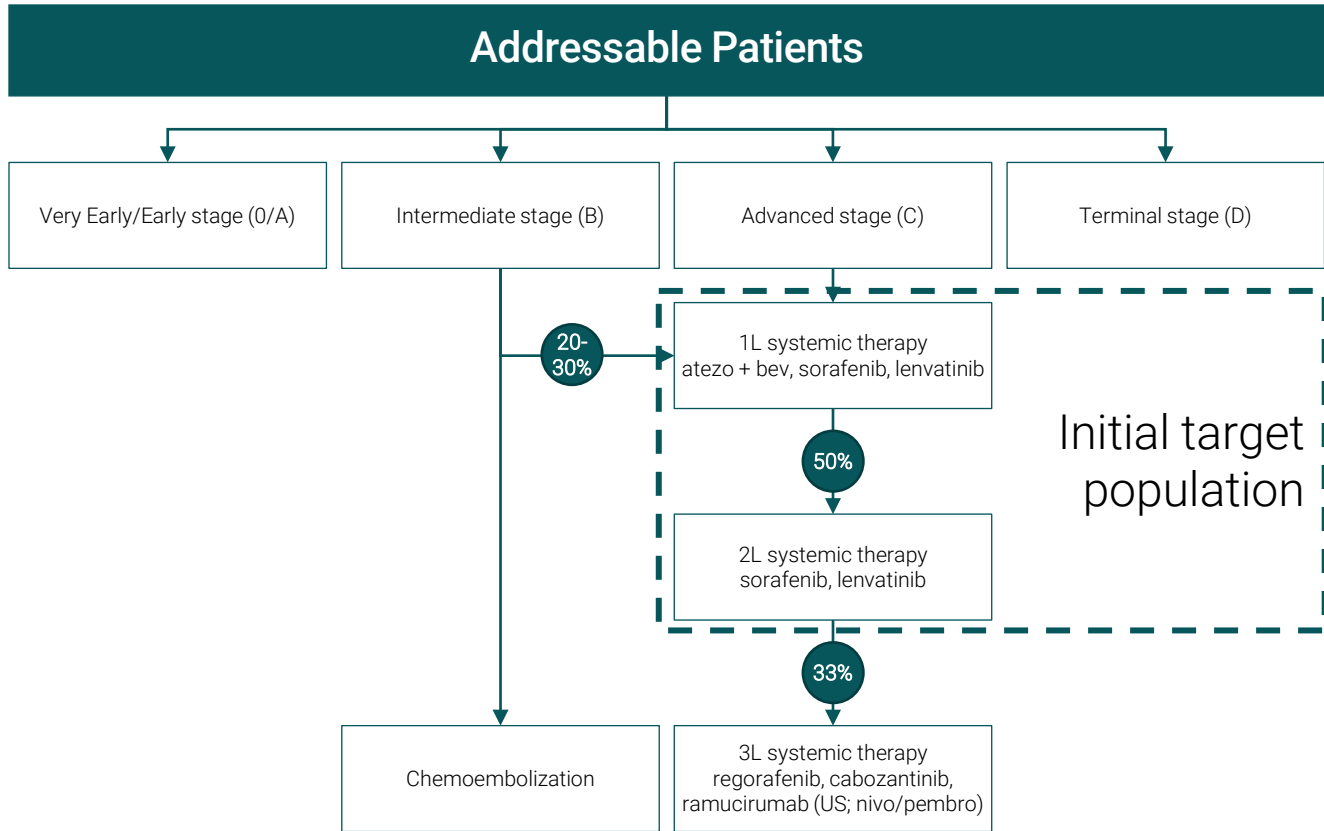
# MIV-818/fostroxacinabine bralpamide

– *treatment landscape of advanced HCC*





# HCC Epidemiology and treatment algorithm



- Estimated treatment duration ~10+ months
- Majority of alternatives only approved for Child-Pugh Class A patients (~45%)
- ~40% of patients not eligible for atezo/bev combination

- Estimated treatment duration ~6+ months
- Approximately half of all 1L patients progress to 2L systemic treatment
- Focus for fostroxacitabine bralpamide combinations in phase 1b/2a study

- Treatment duration ~3+ months
- As many as a third of all 2L patients progress to 3L systemic treatment





# Strategic evolution & vision for fostroxacitabine bralpamide in liver cancer

Fostroxacitabine bralpamide; Go-To option for combinations across liver related tumours

## Early lines HCC

Launch as preferred combination partner in select patient groups in early lines HCC with either TKI or PD-1

## BACKBONE IN HCC

Establish as backbone for combinations across HCC with potential for triple combinations & earlier lines

## Beyond HCC

Explore potential in other liver related tumors beyond HCC such as CRC driven liver metastasis

# Clinical portfolio and partnerships




## 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	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, SCC				IP : 2034
MIV-711	Cathepsin K inhibitor	OA <sup>2)</sup>				IP : 2034

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

2) Osteoarthritis

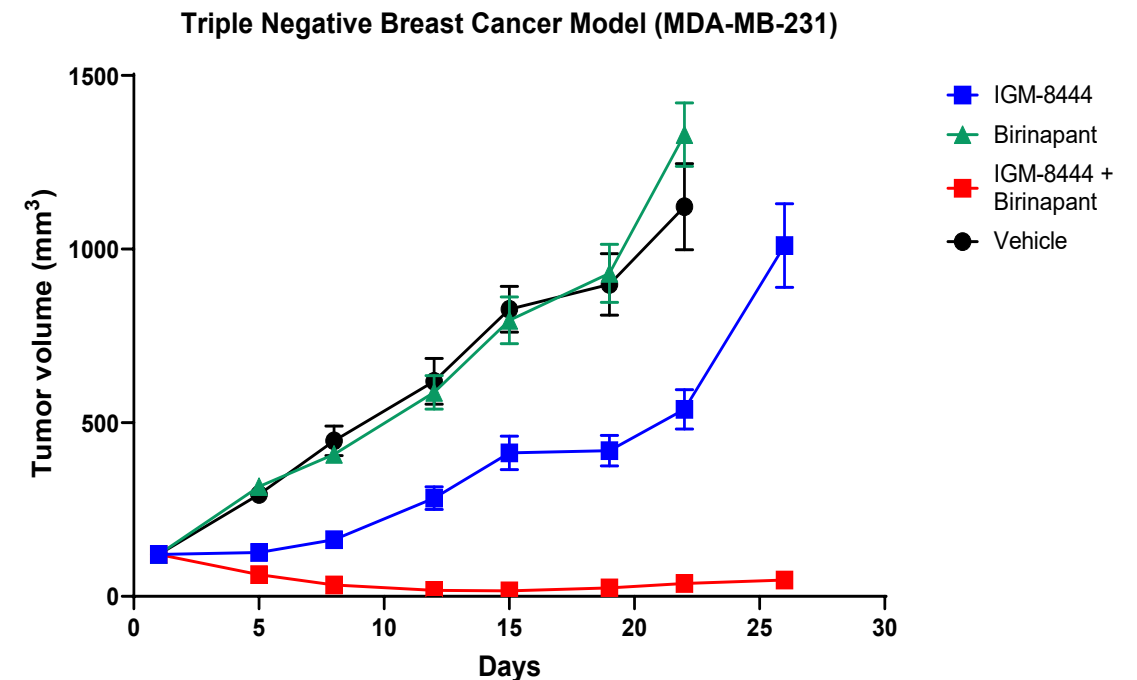
# Birinapant – Licensing agreement with IGM Biosciences

## Licensing agreement with clear upside potential

- IGM is a clinical-stage biotechnology company focused on creating and developing engineered IgM antibodies
- Clinical testing of birinapant (IGM-9427) in combination with IGM-8444, a Death Receptor 5 (DR5) agonist initiated during 2021 in patients with solid tumors\*
- Potential 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 tumours will be in two stages: a dose-escalation stage and an expansion stage (NCT04553692)

## Preclinical models support synergistic anti-tumor activity



# Remetinostat – Efficacy and safety shown in 3 skin cancers

Three phase II trials completed

## Cutaneous T-Cell Lymphoma (MF-CTCL)

- Open label, multicenter Phase II study (60 patients) results showed 40% ORR, and reduced pruritus (itching) in 80% of patients

## Basal Cell Carcinoma (BCC)

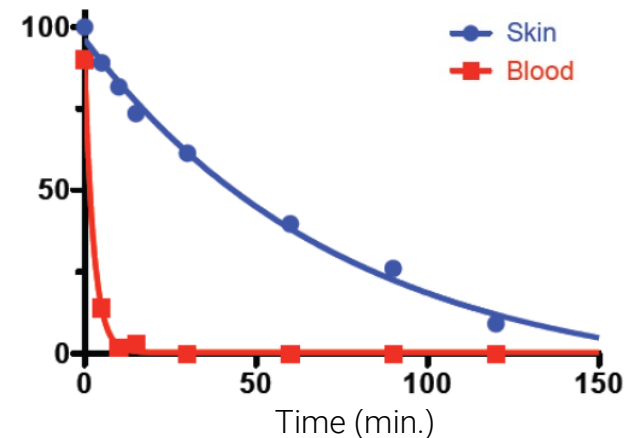
- Open label phase II study (25 patients, Stanford ISS) results showed 70% ORR

## Squamous cell Carcinoma (SCC)

- Open label phase II study (4 patients, Stanford ISS) results showed 100% ORR

Unique topical HDAC-inhibitor

Stability of remetinoastat



- Rapid breakdown by esterases in human blood ( $t_{1/2}$  ~4 mins)
- Negligible levels of systemic exposure translates to reduced risk of HDACi class-associated toxicities

Re-negotiated revenue share agreement with Tetralogic enabling business development potential



# Looking ahead

# Significant progress in 2021 delivering on key strategic priorities; more to come

## Key progress made in 2021

## Potential future key events

### Accelerating fostroxacitabine bralpamide

- Phase 1b monotherapy data presented supporting continued development
- Decision to continue development as combination therapy & Phase 1b/2a combo study initiated with Keytruda® or Lenvima®
- MIV-818 awarded INN fostroxacitabine bralpamide, highlighting its unique MoA

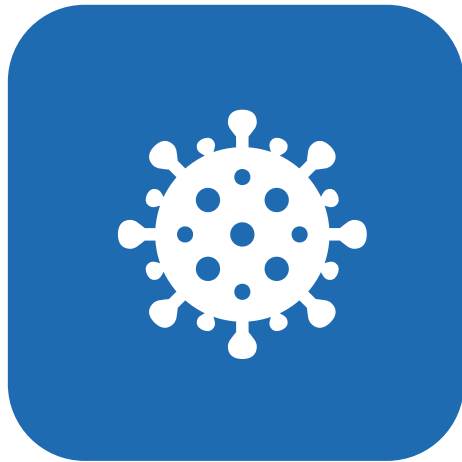
- First safety data from phase 1b combo study in Caucasian & Asian patients
- Initiation of phase 2a dose expansion study with one or two combination arms
- First efficacy data from combination arm(s)
- Initial steps to prepare for IND filing
- Asia development plan

### Maximise value of assets for partnering & out-licensing

- Initiation of clinical study with birinapant + IGM-8444 (DR5) in patients with solid tumors
- Re-negotiated deal for remetinostat improving Business Development potential
- Reteminostat data published in both BCC & SCC, further supporting BD potential

- Birinapant + IGM8444 first data & decision which tumors to continue development in
- CD selection and IND-filing for USP-1 by Tango
- Value added partnering opportunities for remaining assets

# Medivir – transformation journey well underway



**Focused strategy with clear priority & momentum for exciting lead asset**



**Experienced & engaged management team & board**



**Remaining assets either out-licensed or re-negotiated to enable valued adding deals**



# Q&A