

A laboratory setting with a pipette and two racks of multi-well plates containing small vials. The scene is dimly lit with a blue glow from the plates. The pipette is positioned above the plates, and the vials are arranged in neat rows.

# MEDIVIR

## Carnegie Nordic Healthcare Day

December 2017

# Important notice

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# Improving life for cancer patients through transformative drugs

- Utilizing a **world-class scientific platform** to bring new therapies to cancer patients
- **Cutting-edge expertise** in NUCs<sup>1</sup> and protease inhibitor design
- Delivered **successful products** from idea to the market
- Strong commercial focus – Delivered more than **20 global partnerships**
- **Clinical pipeline** composed of projects with **multi-billion dollar sales** potential as well as **orphan drug candidates**

## Basic facts

- Headquarters in Huddinge, Sweden
- 76 employees, 43 with PhDs
- Listed on the Nasdaq Stockholm, ticker: MVIR
- Current market capitalization: SEK 1,200m (USD 140m)<sup>2</sup>
- Website: [www.medivir.com](http://www.medivir.com)



# Oncology drug development in areas of high unmet need

Strong pipeline...

Project, Mechanism	Disease area	Preclinical phase		Clinical phase		
		Discovery	Preclinical	Phase I	Phase II	Phase III
<b>Remetinostat</b> Topical HDAC inhibitor	<b>Early-stage cutaneous T-cell lymphoma</b>	[Progress bar: Discovery to Phase II]				
	<b>Basal cell carcinoma</b> (Stanford investigator sponsored study)	[Progress bar: Discovery to Phase II]				
<b>Birinapant</b> SMAC mimetic	<b>Solid tumors</b> (combo with Keytruda®)	[Progress bar: Discovery to Phase I]				
	<b>High-grade serous carcinomas</b>	[Progress bar: Discovery to Phase I]				
<b>MIV-818</b> , Nucleotide DNA polymerase inhibitor	<b>Hepatocellular carcinoma</b>	[Progress bar: Discovery to Preclinical]				
<b>Leukotide</b> , Nucleotide DNA polymerase inhibitor	<b>Hematological cancers incl. acute myeloid leukemia</b>	[Progress bar: Discovery]				
<b>MIV-711</b> Cathepsin K inhibitor	<b>Osteoarthritis</b>	[Progress bar: Discovery to Phase II]				
<b>MIV-323</b> Fusion protein inhibitor	<b>RSV-infection</b>	[Progress bar: Discovery]				

Cancer

...leveraging specialist drug discovery expertise

**Protease inhibitors**  
(primary focus: deubiquitinases)

**Nucleoside prodrugs**  
(primary focus: targeted delivery)

■ Protease related  
■ Nucleot(s)ide related

**MEDIVIR**

# Medivir's pipeline projects

1 Remetinostat

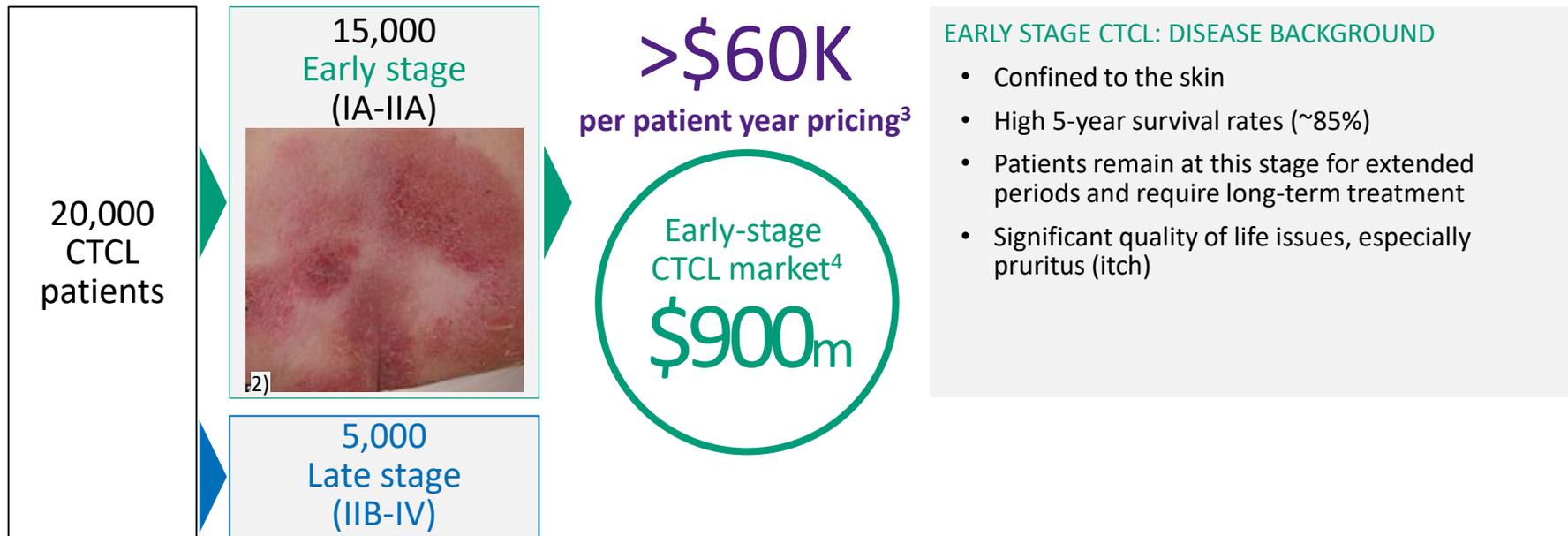
2 Birinapant

3 MIV-711

4 Preclinical / discovery

# CTCL: orphan blood cancer with significant market opportunity

## US CTCL patients<sup>1)</sup>: orphan disease



## Final Phase II data: Confirmed efficacy on skin lesions and reduced itching

### Study design

- 60 patients with stage IA-IIA MF were randomized into three dose arms and treated for up to 12 months
- Index lesions were identified at baseline and assessed throughout the study
- The primary end-point was the proportion of patients with a complete or partial confirmed response assessed using the Composite Assessment of Index Lesion Severity (CAILS)

### Results

- Patients in the highest dose group had the highest proportion of confirmed responses (40%), including 1 complete response
- A positive effect was also seen on the severity of pruritus, a secondary objective in the trial

Dose	Once Daily	Twice Daily	
	1% (n=20)	0.5% (n=20)	1% (n=20)
<b>Lesion Outcomes</b>			
CAILS Confirmed Overall Response Rate (ORR)	4 (20%)	5 (25%)	8 (40%)
Median Duration of CAILS Confirmed Response <sup>1</sup>	2 months	3 months	7 months
<b>Pruritus Outcome</b>			
Patients with clinically significant pruritus at baseline (VAS $\geq$ 30 mm at baseline)	8/20 (40%)	6/20 (30%)	10/20 (50%)
Confirmed response in patients with clinically significant pruritus at baseline	3/8 (37.5%)	3/6 (50%)	8/10 (80%)

<sup>1</sup>) Estimated from visit dates, censored at study end Note: M Duvic *et al.*, EORTC Cutaneous Lymphoma Task Force Meeting (2017), Abstract O55

# Well tolerated without signs of systemic adverse events

## Results

- Across all the dose groups, retinostat was well-tolerated without signs of systemic adverse effects, including those associated with systemic HDAC inhibitors
- Most patients remained on study for the maximum possible duration
  - Median time on treatment: 332 days (1% 2x/day dose)

Treatment-related Adverse Events seen in ≥1 Patients <sup>1</sup>	Once daily		Twice daily	
	1%	0.5%	1%	1%
Any Adverse Event	11	10	11	11
Pruritus	5	3	1	1
Any Other Skin <sup>2</sup>	9	10	11	11
Infections	3	1	0	0
Skin papilloma	0	0	1	1

# Planned Phase III clinical development for early-stage CTCL

## Design

Phase II data supporting highest dose twice daily for Phase III

- Dose response: CAILS ORR & pruritus VAS responses
- A balanced safety profile across all three doses
- Minimal systemic exposure, even at the top dose

One Phase III study expected to be sufficient for NDA

- Past approvals in CTCL were based on pivotal clinical studies involving <260 patients
- Focus on treatment-experienced patients where the medical need is high

## Program Timing

- Phase II final data reported (EORTC CLTF Meeting, 2017)
- End of Phase II discussions with the FDA to enable Phase III

## Costs

- ~\$50m (SEK 400m) expected costs to NDA submission over a 3 year period (incl. Phase III study and third party milestones)

**“As a topical, skin-specific HDAC inhibitor, retinostat has the potential to be efficacious and have an improved safety profile compared to other available treatments.”**

*Youn Kim M.D., Stanford  
University Medical Center, USA*

# Medivir's proprietary pipeline projects

- 1 Remetinostat
- 2 Birinapant
- 3 MIV-711
- 4 Preclinical / discovery

# Despite immuno-oncology breakthroughs patients have unmet needs

Multi-billion dollar market,  
and growing for immuno-  
oncology agents

Revenues of  
PD-1 inhibitors <sup>1)</sup>

**\$6.5bn**

**< 1/2**

of patients derive  
meaningful clinical  
benefit in approved  
indications

**0%**

ORR in other indications  
such as MSS colorectal  
cancer

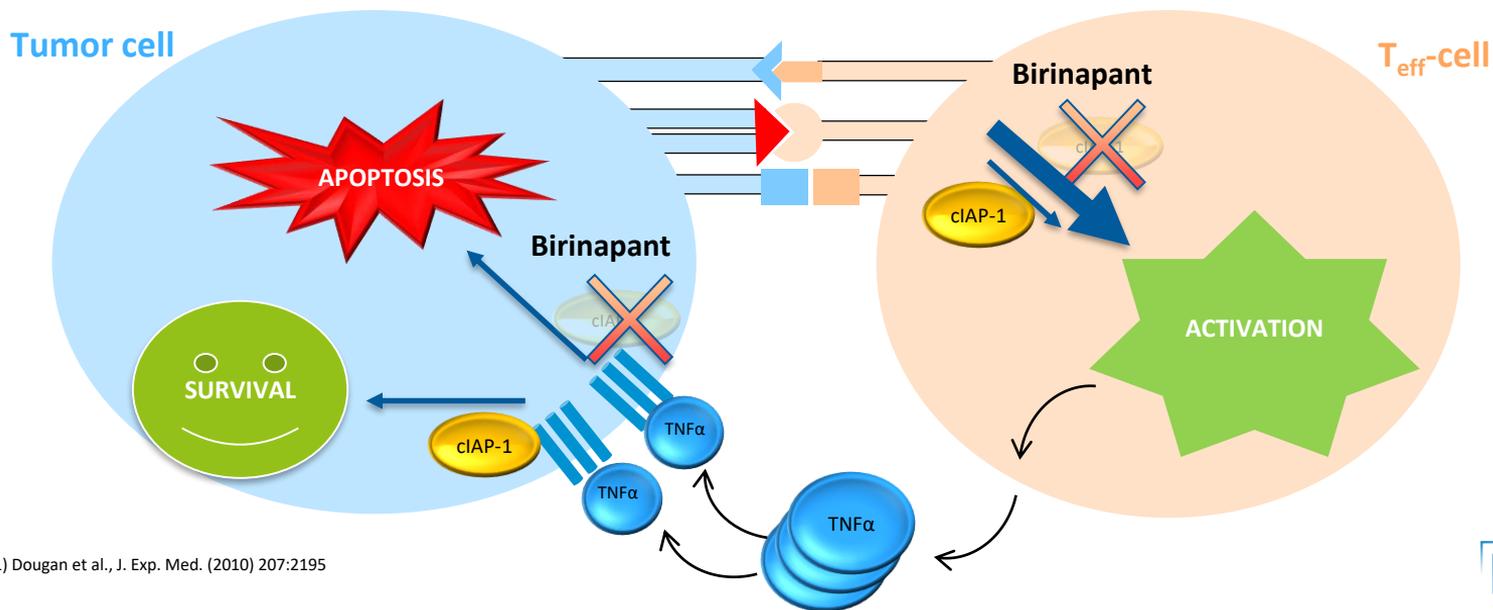
Combination  
regimens to  
enhance benefit  
in underserved  
patients



# Potential to enhance patient response with immune-oncology therapies

## Uniquely potent molecule against a novel target

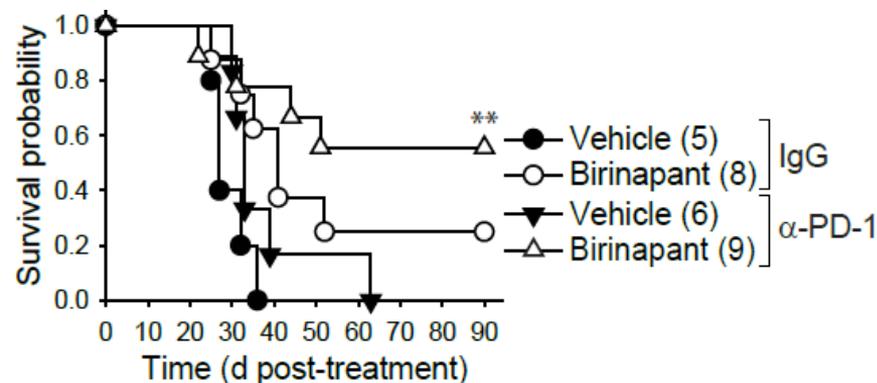
- Only bivalent SMAC (second mitochondrial activator of caspases) mimetic in development
- Targeting of cIAPs results in dual action on T-cells and tumor cells, enhancing cancer cell death



# Activity complements existing therapies

## Immuno-oncology: Strong rationale for combination with Keytruda®

- Recent publications confirm that the combination of a cIAP antagonist, such as birinapant, and an anti-PD1 mAb has enhanced activity in preclinical solid tumor<sup>1</sup> and multiple myeloma models<sup>2</sup> compared to either agent alone



# Birinapant/Keytruda® combination: Phase I/II Study underway

## Collaboration with



- Development collaboration for the Phase I/II study in solid tumors
- Keytruda® provided at no cost
- Joint Development Committee to oversee the study, bringing Merck's immuno-oncology expertise
- Medivir retains full global rights to birinapant and data

## Costs

- ~\$20m (SEK 160m) expected costs to completion of planned studies (incl. Phase I/II study over 3 years; no third party milestones)

## Design



**Phase I:** Sequential group dose-escalation to determine the dose-limiting toxicity and recommended Phase II dose, in combination with Keytruda®

**Phase II:** Safety and tolerability of the recommended dose of birinapant, in combination with Keytruda® in 3-4 defined disease cohorts

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# No disease-modifying osteoarthritis drug exists today

- Affects >30m adults in the US, and ~240m worldwide
- Disease involves both bone and cartilage
- Current treatments are insufficient focusing on symptom relief only

&gt;2m

US patients

&gt;\$3,000

Per patient

&gt;\$6bn

Annual US market potential<sup>1</sup>

Blockbuster revenue opportunity for a disease-modifying OA drug (DMOAD)

Sources: Hunter et al, Nat Rev Rheumatol, 2014; Reginster et al, Ann Rheum Dis 2013. Losina et al 2014

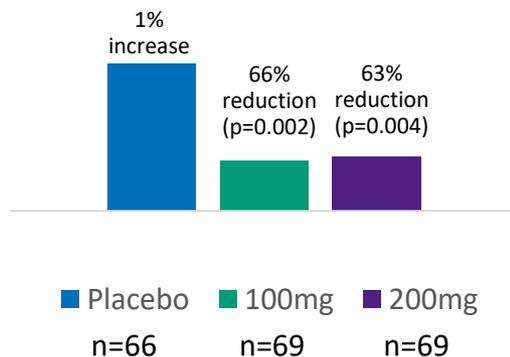
1) >2M adults in US with moderate osteoarthritis in weight bearing joints at annual treatment cost for a drug that impacts disease progression of 3,000 USD/Year (Losina et al 2014)

# Phase IIa data show unprecedented OA disease modification after 6 months

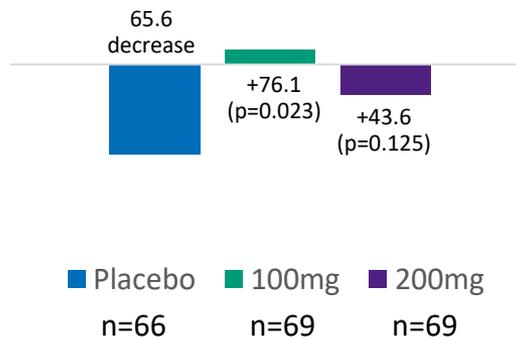
## Benefit on both bone and cartilage

- Increasing joint bone area is a key marker of osteoarthritis and disease progression
- Both MIV-711 doses substantially reduced medial femur bone area growth and loss of cartilage thickness relative to placebo<sup>1</sup>:

### Medial femur joint bone area



### Central medial femur cartilage thickness LS mean (μm)



## Acceptable safety and tolerability profile

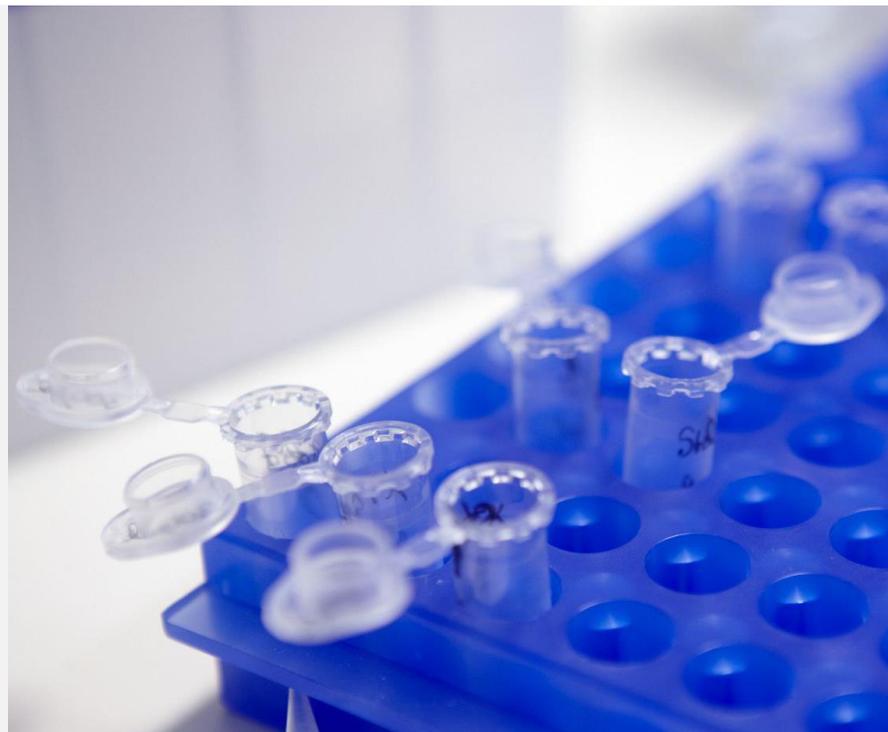
- Both doses showed acceptable safety and tolerability for this patient population
- Six independent DMC meetings held during the Phase IIa program have reviewed unblinded safety data and concluded "continue as planned"

1) <http://acrabstracts.org/> Abstract 14L

## Positive trends across all Pain and other Patient Reported Outcomes

**MIV-711 showed consistent tendency to improve patient-reported symptoms, including pain, however did not reach statistical significance**

- A tendency was observed favoring both the 100mg and 200mg groups for patient-reported pain on the NRS scale (the primary endpoint)
- This tendency was observed consistently across other patient-reported symptoms such as:
  - Daily reporting of pain in E-diaries
  - Measures of pain associated with the daily activities
  - Satisfaction with the function of the diseased knee
- The findings on pain and other clinical symptoms from this study will enable the design of future, longer, studies aimed at demonstrating the effects of MIV-711 on both joint structure degeneration and pain and other clinical symptoms

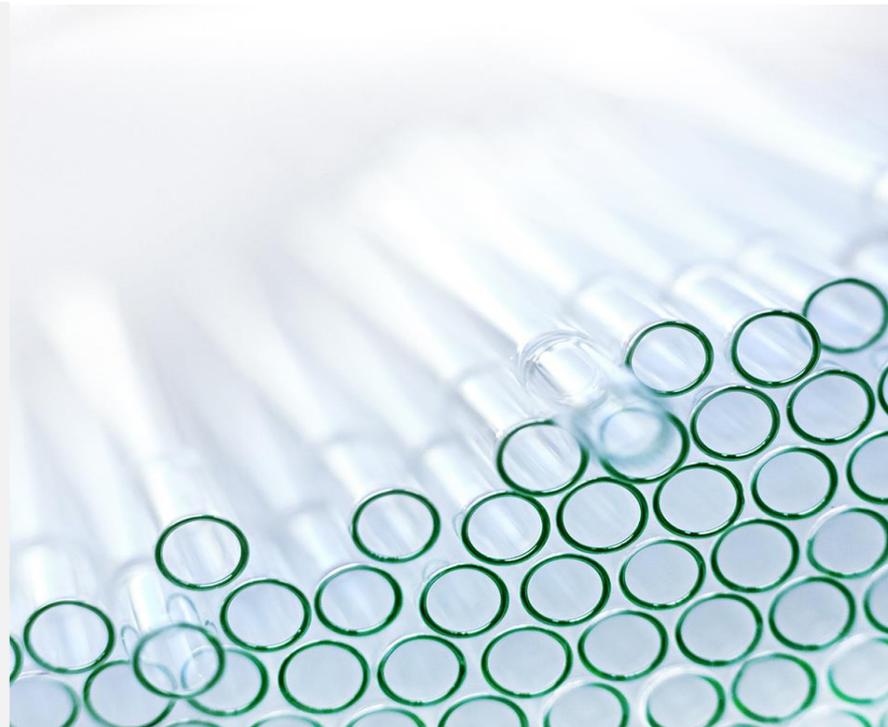


## Continuing to advance MIV-711 development

- Phase IIa data presented in the late-breaker session at the 2017 Annual Meeting of American College of Rheumatology (November 3-8)
- Fast track designation granted by FDA (October 24)
- Partnering discussions ongoing
- Additional 12 and 6 month efficacy data from extension study expected 1H'18

“The finding that MIV-711 slows the degenerative changes on both bone and cartilage in knees affected by OA is an enormously exciting finding”

Professor Philip Conaghan, Professor of Musculoskeletal Medicine at the University of Leeds, UK, and lead investigator on the MIV-711-201 study



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# Drug discovery expertise: Nucleoside Prodrugs & Protease Inhibitors

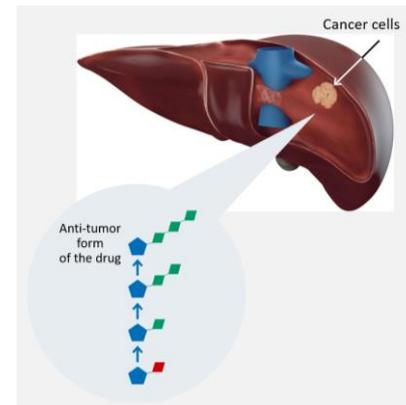
## MIV-818: Liver-targeted nucleotide prodrug for advanced liver cancers

- New chemical entity based on active agent troxacitabine using Medivir's nucleoside prodrug expertise
- Direct targeting to the liver to improve both efficacy and safety with opportunities in combination or as a standalone drug

### Phase I expected to start 2018

- Pre-clinical safety ongoing; topline data expected YE 2017

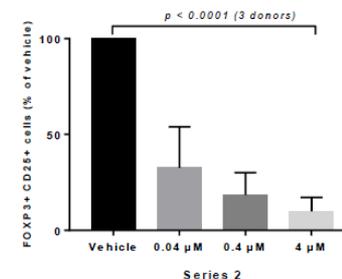
### Market exclusivity with full NCE patent protection



## TRIP: T<sub>reg</sub> inhibitor project for immuno-oncology

- A novel biological target enabling selective suppression of T<sub>reg</sub> cells
- IP filed on the target itself and two classes of small molecule inhibitors
- Small molecules with highly potent compounds (K<sub>i</sub> values <15 nM against the molecular target)
- Increase of T<sub>eff</sub>/T<sub>reg</sub> cell ratio demonstrated *in vitro* and *in vivo*

Impact on Treg differentiation



# Why Medivir?

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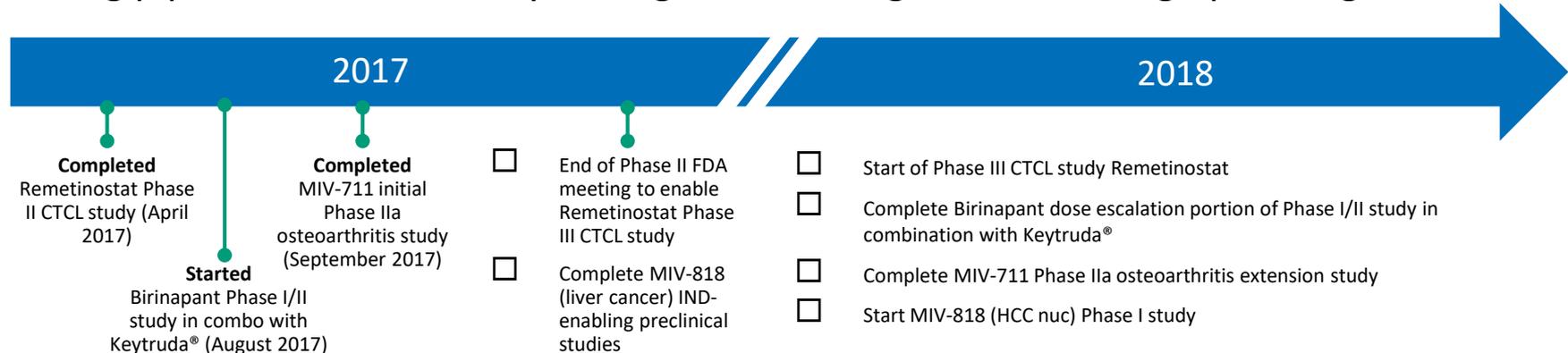
- Track record of delivery

3 candidate drugs into development in 2 years

2 products from idea to market

>20 global partnerships, multiple repeat partners

- Strong pipeline from discovery through clinical stages with exciting upcoming news flow



- Near-term opportunity to generate revenues through partnership