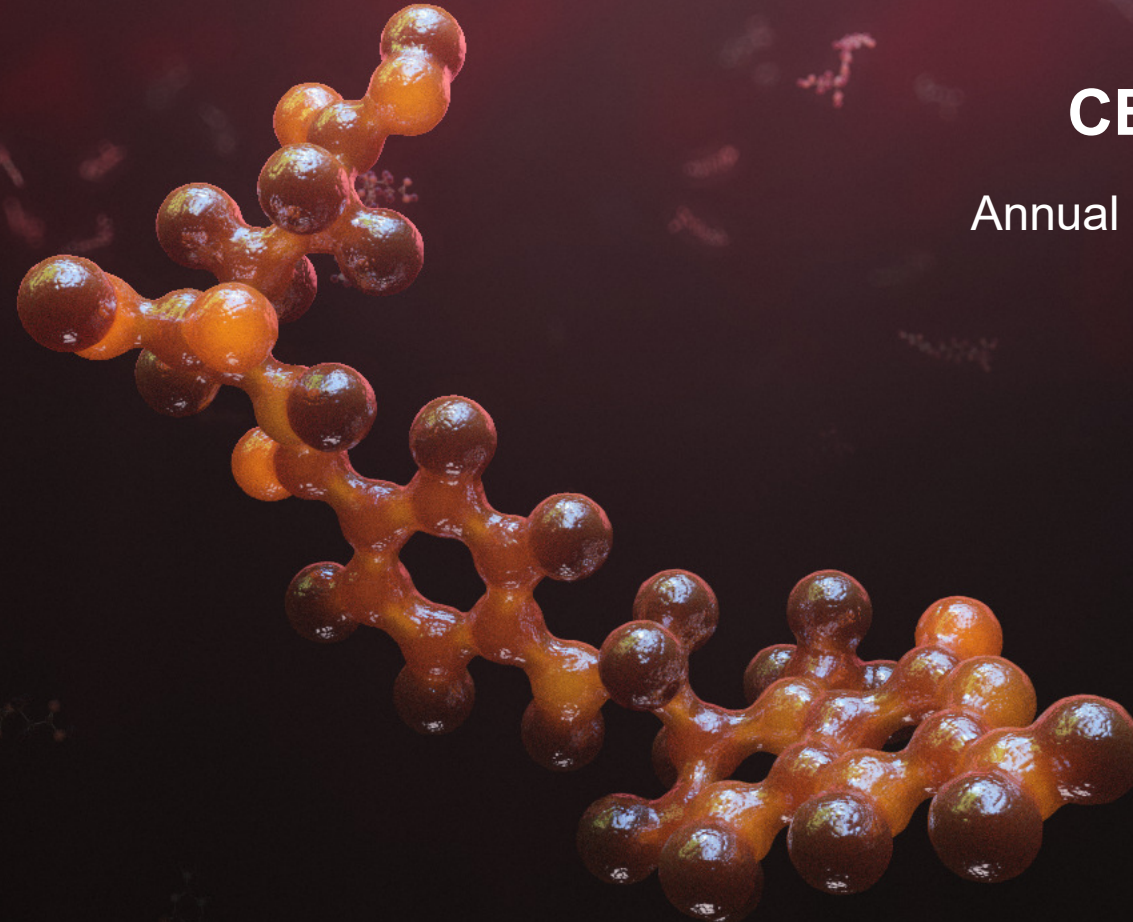




# CEO presentation

Annual General Meeting 2019



# Company Overview

## Isofol in short

- Isofol is developing arfolitixorin for the treatment of colorectal cancer (CRC) the 3rd most prevalent cancer with 2nd highest mortality rate
- Blockbuster potential (more than 370 000 patients in the 7MM) based on arfolitixorin's potentially superior clinical benefit and easy substitution for current Standard of Care
- Recently initiated global pivotal Phase 3 - study (AGENT) with arfolitixorin in first line metastatic colorectal cancer (mCRC) - readout expected in 2021
- Arfolitixorin is intended to improve 5-FU based chemotherapy by directly providing MTHF (6R,5-10 Methylene tetrahydrofolate acid) essential for TS inhibition leading to more effective tumor shrinkage and increased progression free survival (PFS)
- This opens up for label extension into other cancer indications where 5-FU is widely used – Pancreatic-, Breast-, Head and Neck-, and Gastric Cancer
- Commercial grade CMC process in place and valid patents until 2037 in the U.S., 2034 in RoW
- Isofol is led by an experienced team and Board of Directors

## Company Snapshot

Listing venue	Nasdaq First North Premier
Ticker	ISOFOL
IPO	April 2017 (SEK 430m primary)
Cash position <sup>1)</sup>	SEK ~245 (~ €224 million),
Company founded	2008
Headquarters	Gothenburg
No. of employees	14
Total investment to date	SEK ~650m

1) As of March 31, 2019.

# Clinical & Commercial opportunity

---

Arfolitixorin is intended to improve established therapies

# Arfolitixorin has the potential to increase efficacy of current standard of care chemotherapy

- Arfolitixorin is the first pure form of MTHF – the active substance

**The Problem:** Existing 5-FU + MTHF treatment with the pro-drug leucovorin – up to 2/3rds of patients might not effectively produce the active metabolite



**Problem with current LV based regimen:**

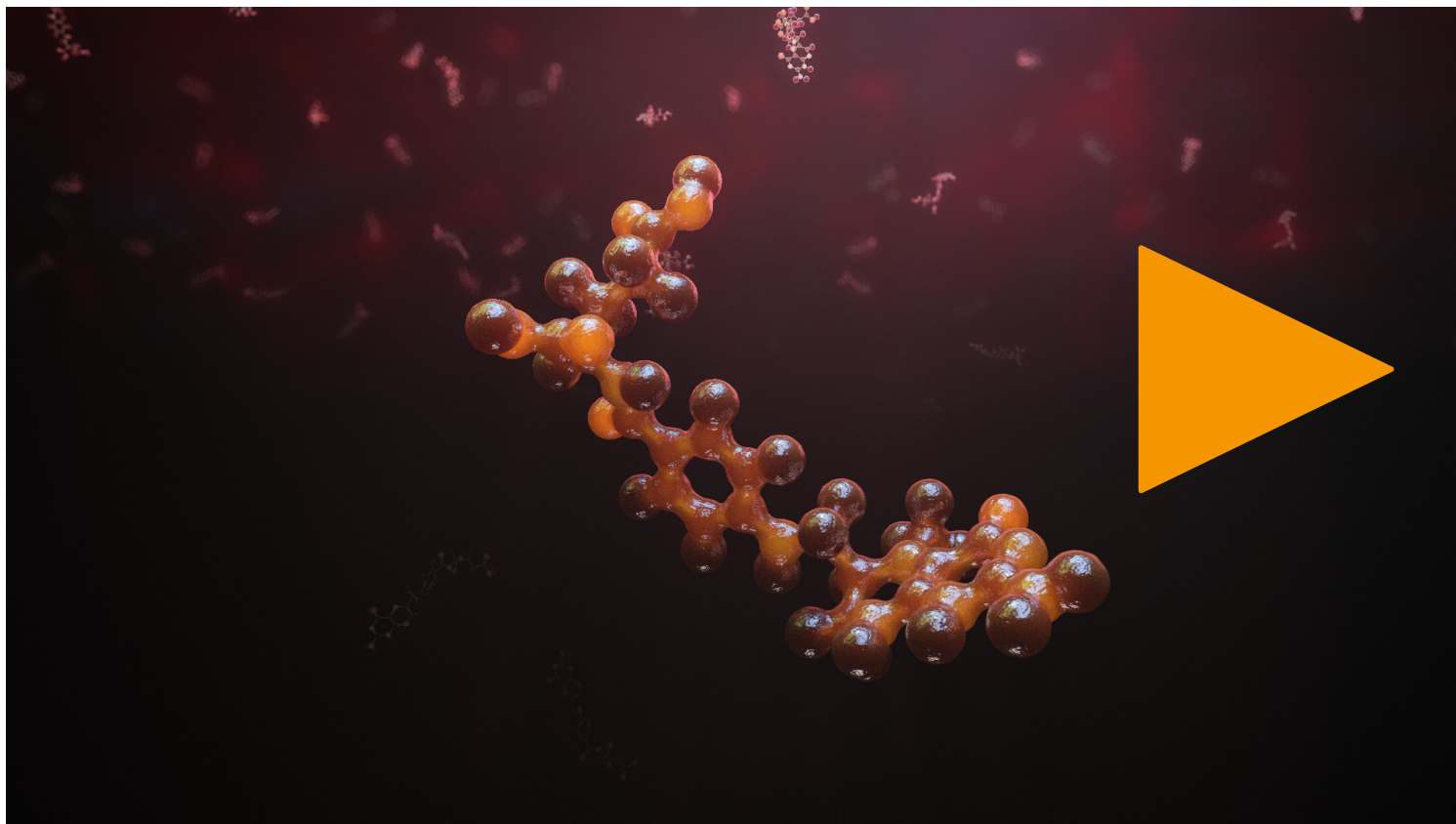
- Up to 2/3 of patients may not be able to convert to MTHF efficiently
- Less than 50% responding to current SOC
- MTHF essential for 5-FU anticancer effect

**The Solution:** Novel 5-FU + MTHF treatment with the active substance - arfolitixorin



# The mechanism of action - animation

---



# Arfolitixorin Represents a Significant Commercial Opportunity

---

- **Large Patient Population:**
  - Colorectal Cancer (CRC) is 3<sup>rd</sup> most common cancer and 2<sup>nd</sup> highest mortality
  - 1.8 Million annual patients diagnosed globally
- **Arfolitixorin in First Line Treatment:**
  - Significant advance in first line therapy for CRC, no new drugs approved during the last 15 years
  - Relevant for all CRC chemotherapy patients and not limited to genetic subtypes
  - PD-1 inhibitors are only active in ~ 4% of the mCRC population (MSI-high)
- **Straightforward adoption into Standard of Care:**
  - Physicians in 7 major markets recognize the value proposition and willing to switch significant market share to arfolitixorin (30-50%)
  - Straightforward switch with no changes to existing chemotherapy regimens
  - Large potential clinical benefits and patient survival outcomes
- **Premium Pricing:**
  - Three independent market research studies have confirmed premium pricing expectations

According to primary market research, Arfolitixorin has potential for greater than \$1B in peak sales in the 7 Major Markets in 1<sup>st</sup> line mCRC only<sup>1</sup>

# Financial Report

---

Arfolitixorin is intended to improve established therapies

# Financial report - 2018

	2018	2017
<b>Consolidated Income Statement</b>	<b>IFRS</b>	<b>IFRS</b>
Other Operating Income	0	227
External Costs	-72 116	-61 210
Personnel Expenses	-17 576	-11 587
Depreciation	-157	-157
Other Operating Expenses	0	140
<b>Operating loss</b>	<b>-89 849</b>	<b>-72 587</b>
Net Financial items	6 724	552
<b>Loss After Financial Items</b>	<b>-83 125</b>	<b>-72 035</b>
	<b>31/12</b>	<b>31/12</b>
	<b>2018</b>	<b>2017</b>
<b>Consolidated Balance Sheet</b>	<b>IFRS</b>	<b>IFRS</b>
Total Fixed Assets	4 092	481
Total Current Assets	284 460	360 795
Total Assets	288 552	361 276
Total Equity	265 008	343 033
Total Current Liabilities	23 544	18 243
Total Equity and Liabilities	288 552	361 276
Solidity	92%	95%
Average Number of employees	10	9

- The incentive programme “2012” with stock and employees options was wound up in January 2018. 450,302 shares were subscribed for at SEK 17 per share by the company's CEO, Members of the Board, and employees.
- External Costs increased by TSEK 11 046 and relates to higher activities within clinical studies (ISO-CC-005 and ISO-CC-007) and commercialization.
- Personnel Expenses increased by TSEK 5 989 and relates to higher costs due to increased number of employees and personnel being employed for the full year 2018 compared to part of 2017. Number of employees amounted to 11 at year-end.
- Net Financial Items increased by TSEK 6 172 and mainly relates to positive currency exchange effects for USD and EUR.
- At year-end Cash and Cash Equivalents amounted to TSEK 272 897 (357 331). The excess liquidity have been managed within a money market fund which have a low risk profile and low rate of return.
- Cash flow from operating activities amounted to - TSEK 92 458 (-61 943) and the increased cash flow relates to clinical activities, pre-payments to suppliers and costs for commercialization.
- The cash flow for the year and the net Cash position at year-end are in-line with the company's business plan.

# January- March (Q1) 2019

<b>Consolidated Income Statement</b>	<b>Q1 2019</b>	<b>Q1 2018</b>
	<b>IFRS</b>	<b>IFRS</b>
Other Operating Income	0	0
External Costs	-24 789	-19 951
Personnel Expenses	-5 228	-3 937
Depreciation	-362	-39
<b>Operating loss</b>	<b>-30 370</b>	<b>-23 927</b>
Net Financial items	3 404	4 040
<b>Loss After Financial Items</b>	<b>-26 966</b>	<b>-19 887</b>
	<b>31/3</b>	<b>31/3</b>
	<b>2019</b>	<b>2018</b>
<b>Consolidated Balance Sheet</b>	<b>IFRS</b>	<b>IFRS</b>
Total Fixed Assets	9 125	442
Total Current Assets	259 263	344 613
Total Assets	268 388	345 055
Total Equity	239 525	328 246
Total Current Liabilities	28 863	16 809
Total Equity and Liabilities	268 388	345 055
Solidity	89%	95%
Number of employees	14	10

- The incentive programme “2018” with stock options was launched in Q1 2019. All employees took part in the stock option programme, subscribing for a total of 1,260,136 stock options, yielding 1,482,674 tkr in option premiums. Senior executives (5 persons) paying SEK 207,000 per person for the stock options.
- External Costs increased by 4 784 tkr and relates to higher activities within clinical studies (ISO-CC-005 and ISO-CC-007), costs for regulatory preparations in Japan and costs for investor relations and commercialization.
- Personnel Expenses increased by 1 291 tkr and relates to higher costs due to increased number of employees. Number of employees amounted to 14 at end of Q1.
- IFRS 16 Leasing have been implemented in Q1 2019 and have affected the balance sheet by increasing assets and liabilities by approx 4 856 tkr as of 1 January and increased depreciation during Q1 by approx 327 tkr.
- Net Financial Items is positive due to positive currency exchange effects for USD and EUR.
- Cash and Cash Equivalents amounted to 245 823 tkr (341 108). The excess liquidity have been managed within a money market fund which have a low risk profile and low rate of return.
- Cash flow from operating activities amounted to -29 826 tkr (-23 309) and the increased cash flow relates to higher activities within clinical studies and increased number of employees.
- The Cash Flow for the period and the net Cash position at end of Q1 2019 are in-line with the company’s business plan.

# Significant Achievements & Events 2018

---

Arfolitixorin is intended to improve established therapies

# Significant Achievements and Events 2018

---

## Clinical Development

- The pivotal clinical phase III study, **AGENT** was initiated under a US IND and the study is now active in **USA, Canada, and Europe**.
- The ongoing phase I/II ISO-CC-005 – study, in patients with metastasised colorectal cancer (mCRC);
  - Delivered the recommended dose Isofol's candidate drug, arfolitixorin, of 120mg/m<sup>2</sup>.
  - Positive clinical results demonstrated that patients with mCRC in the first line setting, treated with arfolitixorin in combination with 5-fluorouracil (5-FU) with either irinotecan or oxaliplatin was efficacious and safe.

# Significant Achievements and Events 2018

---

## Publications

### Gene Expression data from a retrospective study presented at ASCO

- Patients treated with 5-FU-based chemotherapy and the leucovorin (LV) folate for metastasised colorectal cancer (mCRC) with a high genetic expression level for ABCC3 have an average PFS of 10.1 months, in comparison with a PFS of 6.5 months for patients with a low genetic expression.
- The study shows a clear link between treatment outcomes, measured as progression-free survival (PFS) and expression levels of genes that control folate metabolism and, hence, conversion of LV to the active substance, methylenetetrahydrofolate (MTHF).

### Mechanism of action data from ISO-CC-005 - study presented at ASCO - GI

- An abstract summarising the positive effects of treatment with arfolitixorin concluded that “the lack of need for metabolic activation makes arfolitixorin a better candidate than the currently registered pharmaceuticals, leucovorin and levoleucovorin, for improved outcome of 5-FU-based chemotherapy regimens in mCRC”.

# Significant Achievements and Events after the reporting period

---

## **Regulatory consensus from FDA and EMA**

- Isofol reached unanimity with both the EMA and FDA on the most important parameters when structuring and implementing the pivotal phase III study, AGENT.

## **Patent approval for arfolitixorin in USA**

- A patent covering both the Active Pharmaceutical Substance (arfolitixorin hemisulfate), the pharmaceutical product, and the finished injectable solution for the treatment of cancer patients, was granted for Isofol's drug candidate, arfolitixorin, in the US and is valid until 2037.

# Clinical Development

---

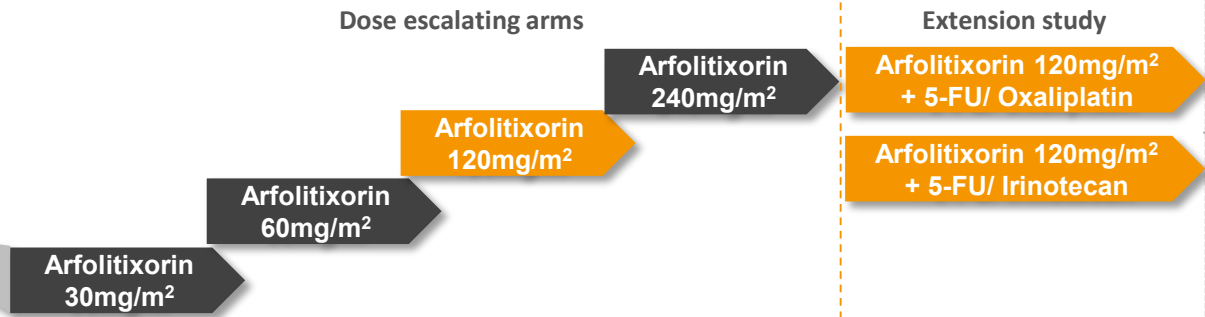
Arfolitixorin is intended to improve established therapies

# Design of the ongoing Phase IIa ISO-CC-005 study

- A safety and dose finding study

## STUDY SUMMARY: ISO-CC-005

mCRC patients  
Any treatment line



Primary Endpoint

**Dose finding & safety**

Secondary Endpoint

**ORR**

Objective response rate

## Structure

### Dose finding part of study (62 patients)

Dose finding study of arfolitixorin at four (4) different dose levels (30 to 240 mg/m<sup>2</sup>) in therapy combinations with the chemotherapeutic agents 5-FU, Oxaliplatin +/- bevacizumab, and Irinotecan.

### Extension cohorts I and II (43 patients initiated)

Extension phase with additional 20+20 targeted patients (1st line) to evaluate safety and efficacy on selected dose regimen of arfolitixorin

**In Total (105 patients)**

## Study sites (preliminary numbers)



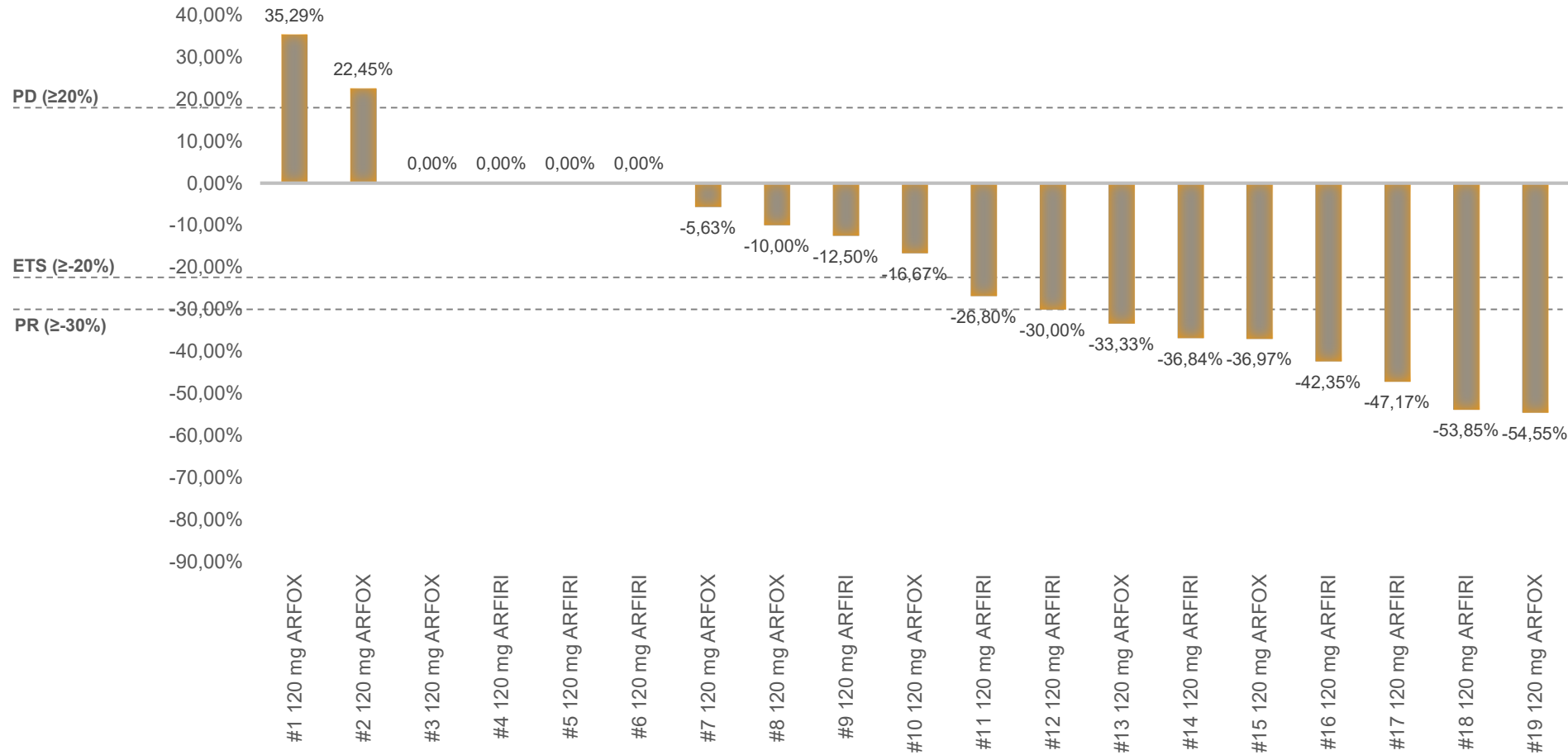
● Number of study sites

89% of patients saw Clinical Benefit

47% Early Tumour Shrinkage ( $\geq -20\%$ ) in 19 first line patients in ISO-CC-005

- Results after 8 weeks treatment with 120 mg/m<sup>2</sup> Arfolitoxorin + 5-FU + irinotecan or oxaliplatin (ARFIRI/ARFOX)

8 WEEKS % CHANGE OF TUMOUR SIZE FROM BASELINE



**Early Tumour Shrinkage (ETS)**

- ▶ 9 patients had  $\geq -20\%$  tumour size reduction
- ▶ ~47% ETS

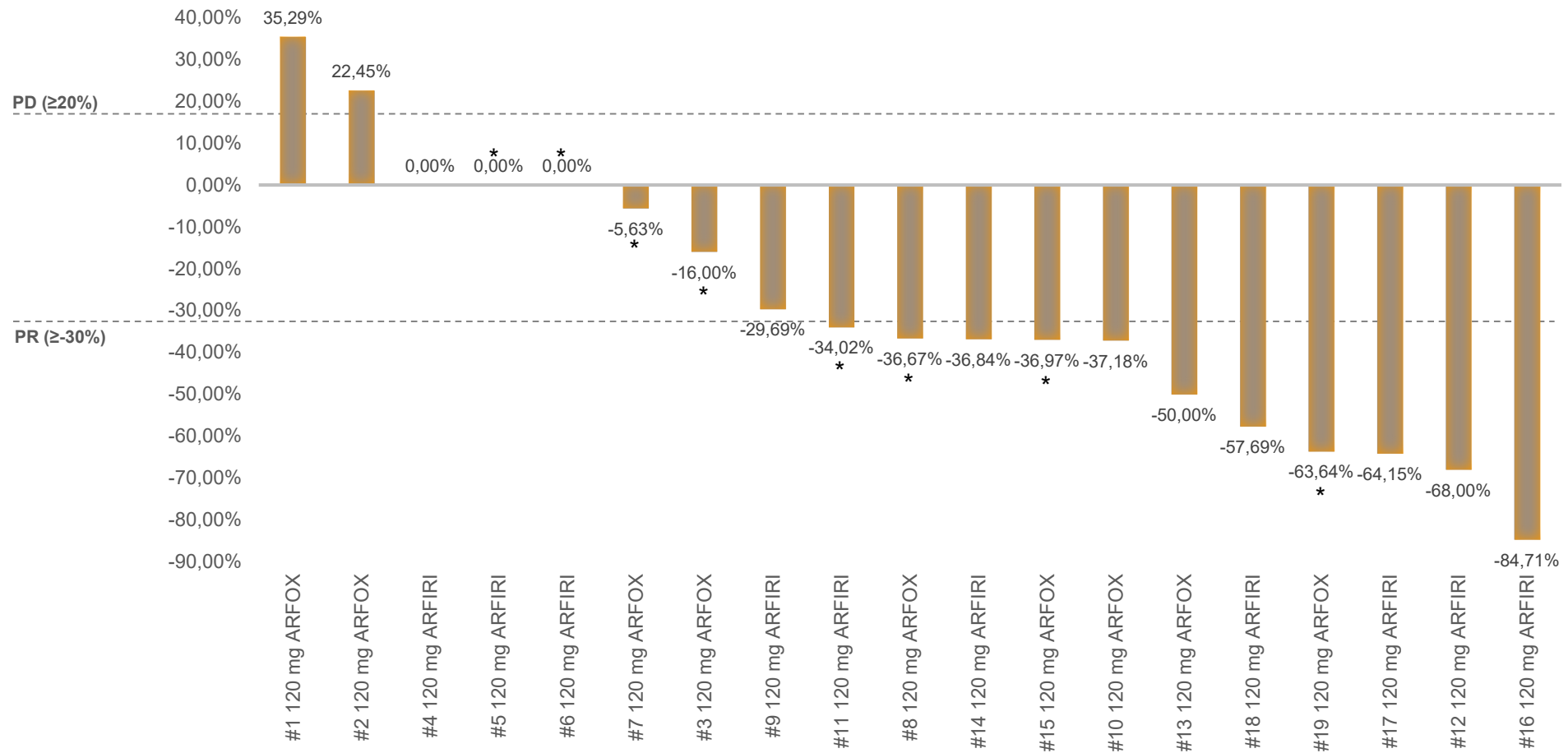
**Clinical Benefit (CB)**

- ▶ 17 out of 19 patients had stable disease, SD (Neither PR nor PD) or partial response, PR ( $\geq -30\%$ )
- ▶ ~89% CB

# 58% Overall Response Rate (≥-30%) in 19 first line patients in ISO-CC-005

- Results up to 32 weeks treatment with 120 mg/m<sup>2</sup> Arfolitixorin + 5-FU + irinotecan or oxaliplatin (ARFIRI/ARFOX)

**% CHANGE OF TUMOUR SIZE FROM BASELINE**



**ORR according to RECIST 1.1**

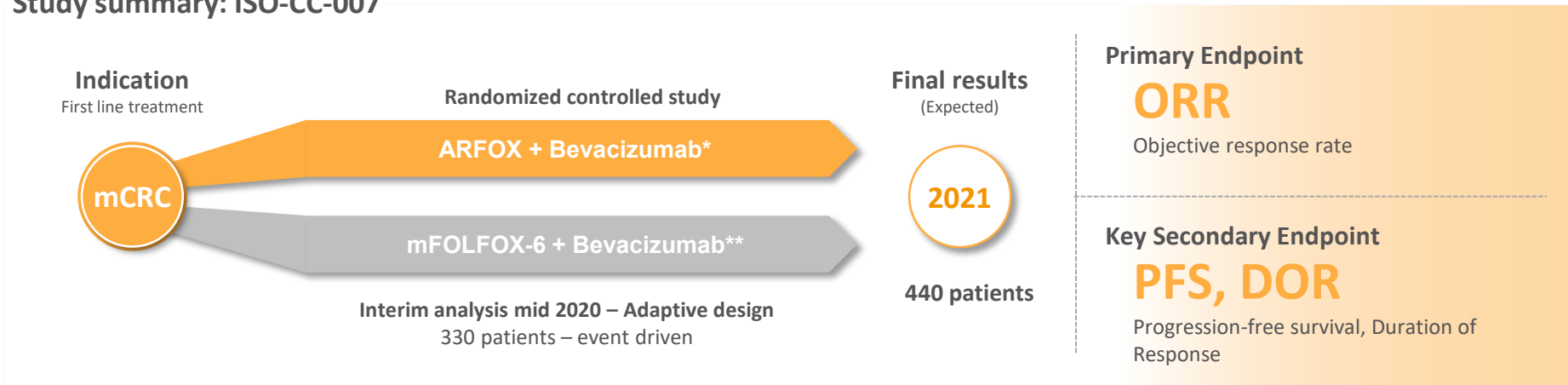
- ▶ **11 out of 19 patients** had partial response, PR (≥-30%)
- ▶ **~58% ORR**

Note: Preliminary unmonitored data and all responses are not confirmed

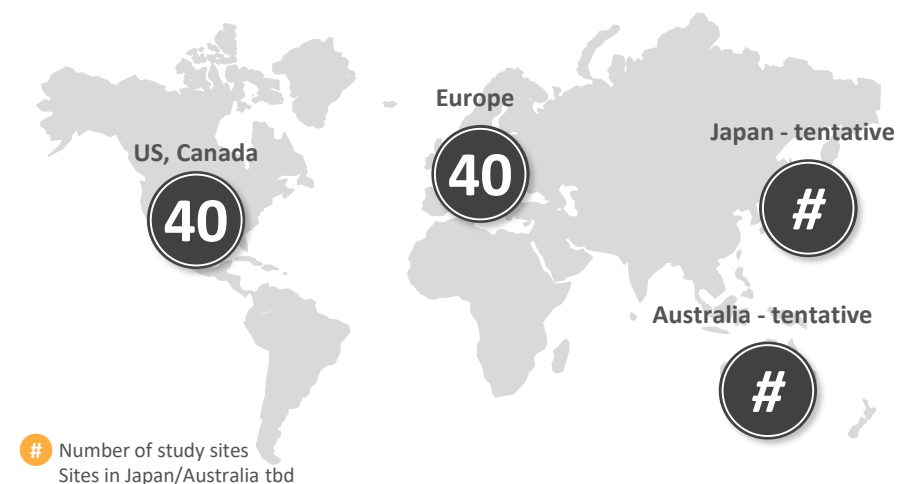
\*Patient received Avastin after 8 weeks of treatment

# AGENT – Ongoing pivotal phase 3 study design

## Study summary: ISO-CC-007



## Study sites



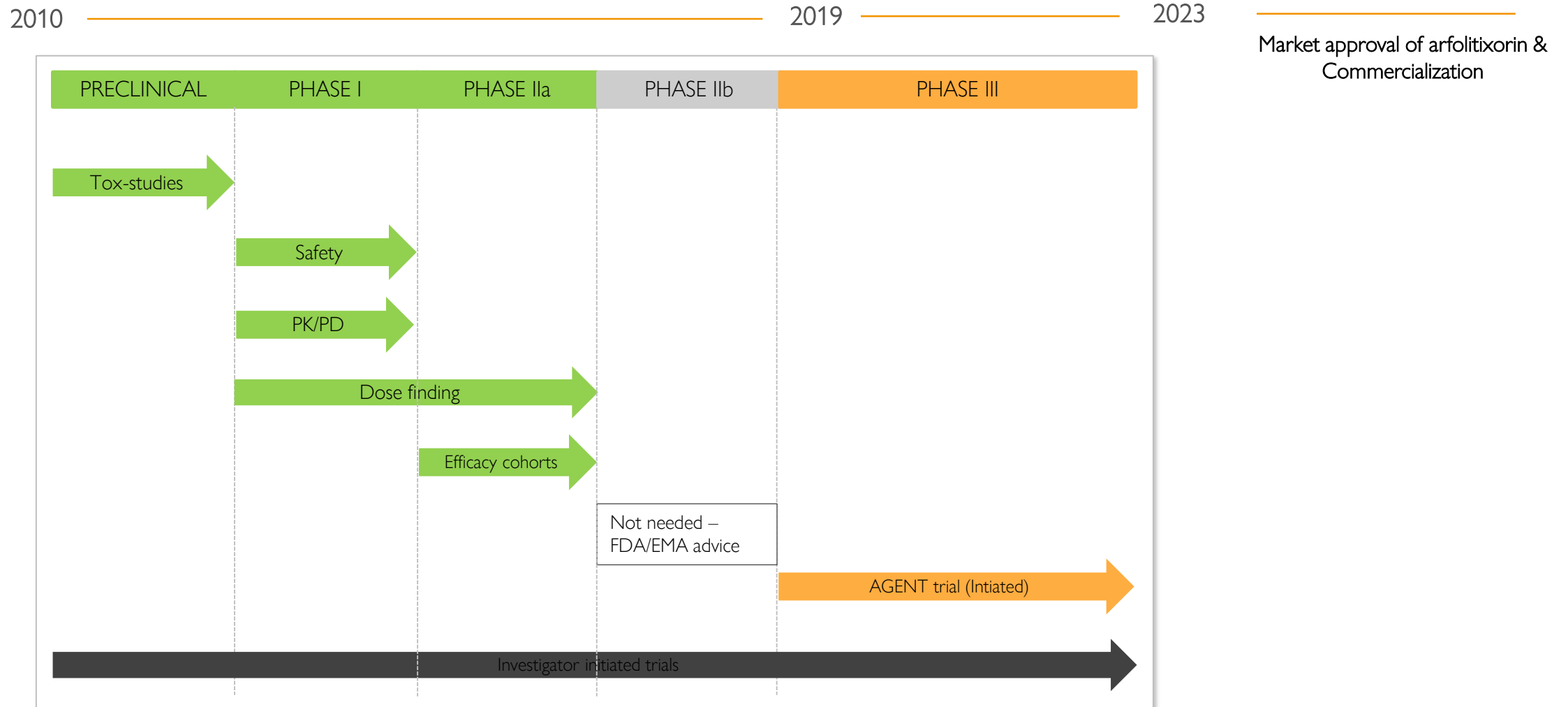
# Time Plan

---

Arfolitixorin is intended to improve established therapies

# Our clinical studies and expected commercialization of arfolitixorin

- Clinical development has been accelerated following strong support from regulatory authorities



# Science, Publications and Key Opinion Leaders

---

Arfolitixorin is intended to improve established therapies

# Science, Publications and Key Opinion Leaders

---

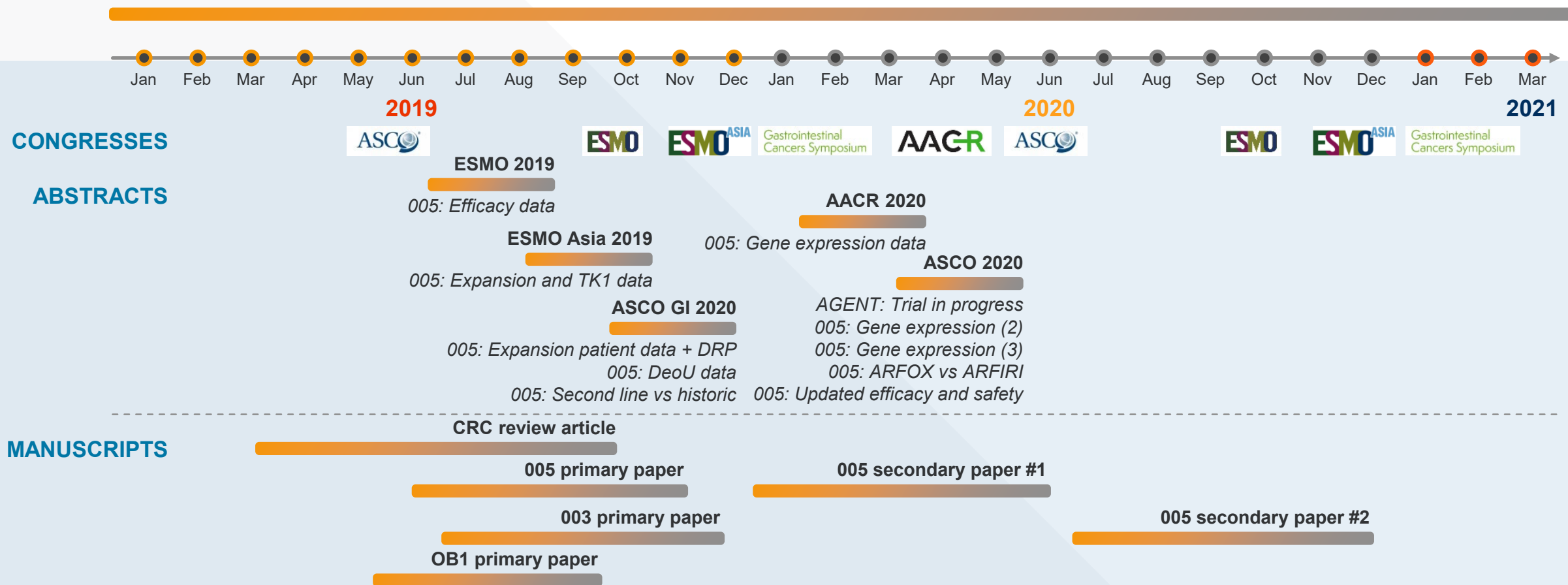
- **Increased focus on “Message development” for arfolitixorin’s key Mode of Action (MOA) adapted for both a clinical and commercial audience**
  - Animal data, PK/MOA, genetic/biomarkers, clinical, safety, marketing/economic, etc
- **Significantly more publications to keep high attention on arfolitixorin development and potential. An updated publications plan has been developed including 25 possible publication targets during the next 3 years:**
  - Own sponsored publications
  - Secondary and competitive publications

**Our aim is to publish 4 primary and secondary publications within the next 6-12 months**

- **Additional external activities with KOLs and Advisory boards have been initiated**
  - Advisory board at ASCO May 31<sup>st</sup> in Chicago with 8 Key Opinion Leaders from US, Europe and Japan
  - Further advisory boards are planned for ESMO Asia, Japanese congress, ASCO GI in San Francisco , AACR, etc

# Publications roadmap

## STRATEGIC MILESTONES



# Organisation

---

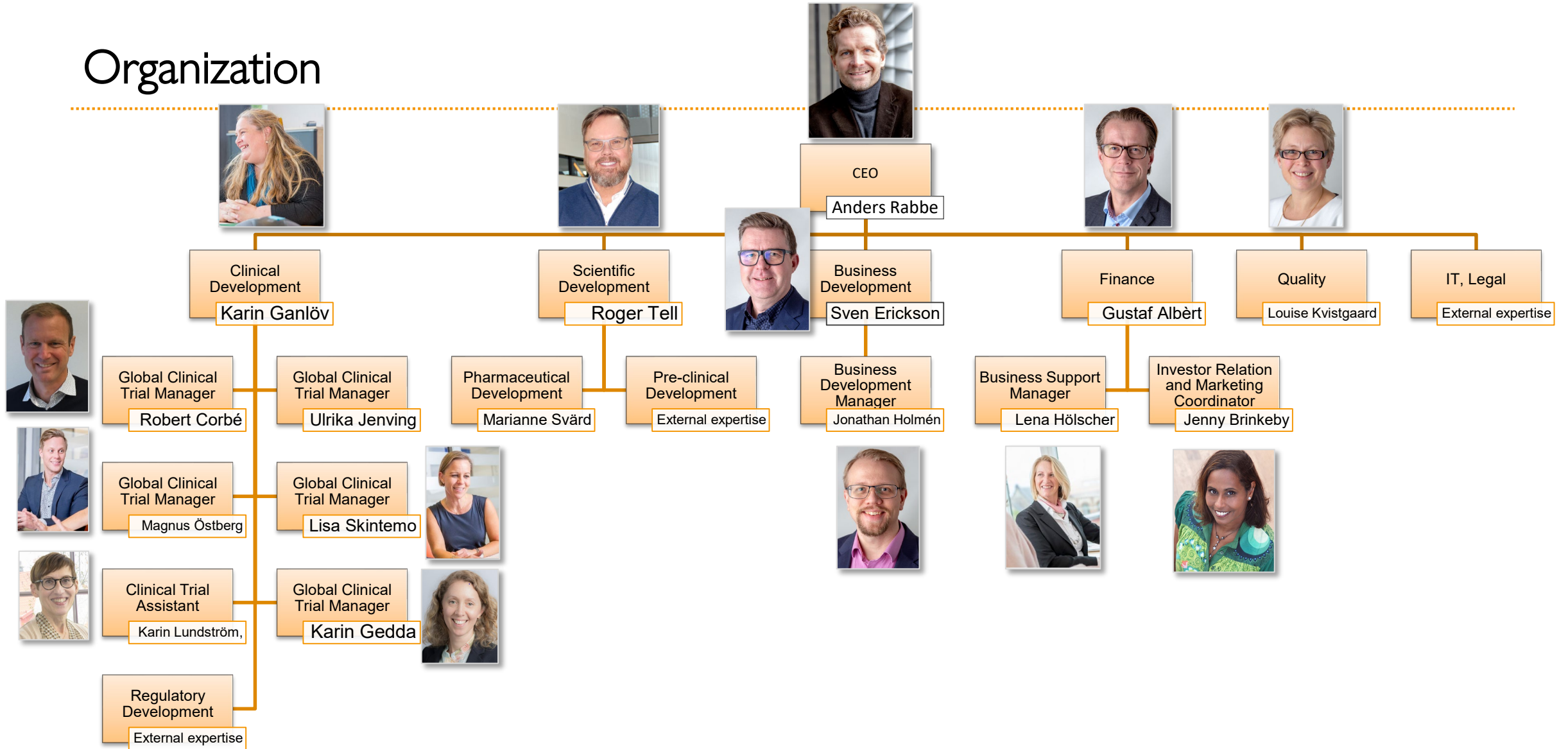
Arfolitixorin is intended to improve established therapies

## Strengthening of the organisation

---

- ✓ Chief Scientific Officer, SVP Clinical Development - Roger Tell, MD, PhD
- ✓ Global Clinical Trial Manager (GCTM) - Ulrika Jenving
- ✓ Business Development Manager (BDM) - Jonathan Holmén

# Organization





**Anders Rabbe, CEO**

[anders.rabbe@isofolmedical.com](mailto:anders.rabbe@isofolmedical.com)



**Ulf Jungnelius, Chairman of the board**

[jungnelius@isofolmedical.com](mailto:jungnelius@isofolmedical.com)



**Isofol Medical AB (publ)**

Biotech Center  
Arvid Wallgrens Backe 20  
SE-413 46 Göteborg, Sweden

[info@isofolmedical.com](mailto:info@isofolmedical.com)  
[www.isofolmedical.com](http://www.isofolmedical.com)