



AGM – CEO presentation

May 2025

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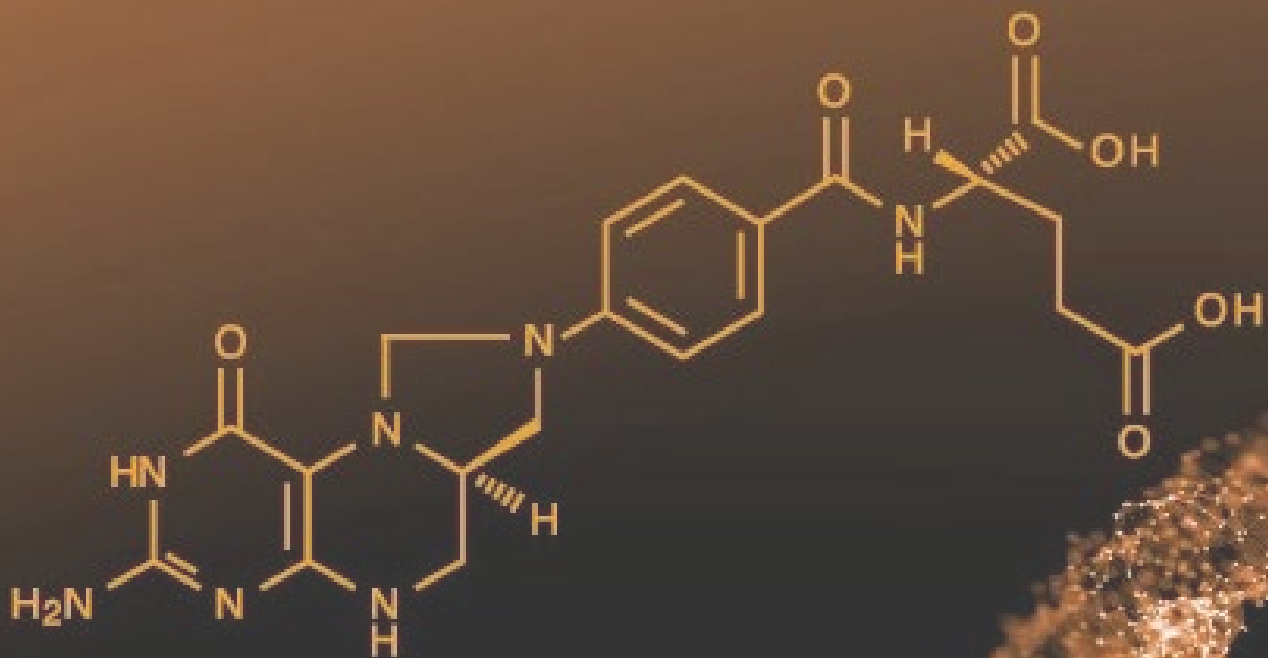
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Moving from
analysis and preparations
in 2024 to
action in 2025.

Now, backed by a solid
evidence platform, focusing
on generating **new clinical
data** in the phase Ib/II trial.

ISOFOL 

2024: A year of analysis and preparations

Building an evidence platform

- Preclinical studies conducted
 - Patient-derived tumoroids
 - Tumor homogenates
 - Liver metastases (Modelle-001)
 - » **Dose-response relationship confirmed**
- AGENT post-hoc analyses concluded
 - » **Per-protocol analysis demonstrating the potential in arfolitixorin**
- White paper on folate pharmacokinetics and MoA produced
 - » **Confirming the rationale for an optimized dosing regimen**

Preparing for action

- Strengthening the team
 - Clin Dev team strengthened in Clin Ops and Regulatory
 - Leadership team enforced (CFO, CMO)
 - » **Setting the team up for the next phase**
- Clinical study preparations
 - Design of phase Ib/II trial concluded
 - Regulatory filings
 - » **Enabling study initiation**
- Partner reengagement
 - Solidifying the partnership with Merck KGaA
 - Reconnecting with Solasia Pharma K.K.

2025: The rubber hits the road

New clinical study

- Phase Ib study being conducted
 - Study approval, site initiation, patient enrollment
 - » **Aiming for rapid data generation**
- Preparations for subsequent steps
 - Preparing for phase II start-up in 2026
 - Phase II solidified and enhanced
 - control arm to be introduced in order to increase the value in the results
 - Adding Japan: PMDA interactions
 - FDA interactions, potential reopening of IND
 - » **Enabling swift transition to ph II and a clear regulatory path to market approval in key regions**

Financing and partnering

- Strengthened relations with Solasia Pharma K.K.
 - Investing 140 msek in arfolitixorin
 - Investing 5 msek in Isofol
 - » **Japanese market secured**
- Further partnering activities initiated
 - » **Preparing for dealmaking**
- Preferential rights issue of units initiated
 - » **Strong interest from shareholders and guarantors**

The basis of Isofol's value creation

**High medical
need**

**Arfolitixorin has
potential to
significantly
improve patient
outcomes**

**High market
potential**

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Isofol's lead indication **metastatic colorectal cancer** is a major medical problem worldwide

1 900 000

people annually are affected

3rd most common cancer

900 000

patient deaths per year

2nd most common cause of cancer death

86 %

of patients with metastatic disease die within five years

▶ **Today's treatments are insufficient.**

The backbone first-line treatment of metastatic colorectal cancer and several other solid tumors is based on chemotherapy

95% of
mCRC
patients:

5-FU

The chemo basis of
cytostatic combinations
(for example FOLFOX)



Folate

Enhances the 5-FU-effect
(today: leucovorin)

arfolitoxin
next-gen folate

ISOFOL 

5-FU + folate will remain the backbone treatment for decades to come

	Phase 2 / Proof-of-Concept	Phase 3 / Pivotal
1L	<ul style="list-style-type: none"> ABBV-400 Deflexifol Onvansertib Ivonescimab Zanidatamab SSGJ-707 	<ul style="list-style-type: none"> PolyPEPI1018 Encorafenib GRANITE-001 Tucatinib
2L	<ul style="list-style-type: none"> MK-7684A SCO-101 Zamaporvint NT-17 TTX-080 Tinodasertib BXQ-350 ADG126 DKN-01 Petosemtamab ETRUMADENANT BOT/BAL MK-1308A 	<ul style="list-style-type: none"> Zanzalintinib
3L	<ul style="list-style-type: none"> E04010 CTX-009 	<ul style="list-style-type: none"> Sotorasib

*“It is **inconceivable to think that 5-FU backbone will not be the mainstay care**, it is a very effective drug within our treatment landscape”*

“I think we are going to get smarter and find more actionable mutations, but I do not think this will impact the 1L SoC”

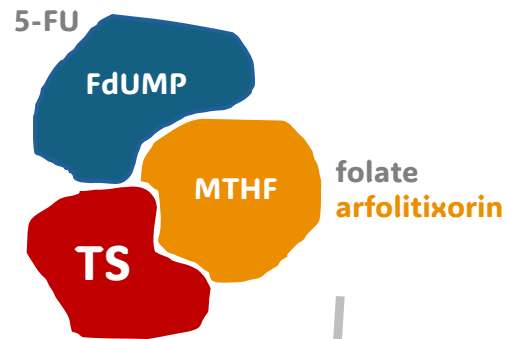
*“**5-FU is the most effective drug in this disease, I don’t think it will ever go away ever**”*

*“There isn’t anything that comes close to chemo or has a response rate high enough to replace the chemo backbone. **5-FU will remain the pyrimidine of choice** in multi-agent chemo regimens in 1L”*

▶ A variety of drugs in development, most intended to be used either as an add-on to 5-FU+folate or in later lines of therapy.

▶ Consensus among clinical experts that 5-FU+folate will remain the mainstay of treatment for the foreseeable future

5-FU + folate targets the TS enzyme to interrupt tumor cell proliferation (MoA simplified)



- Target: **TS** (thymidylate synthase – enzyme central to tumor cell DNA synthesis and proliferation)
- 5-FU is swiftly converted intracellularly to **FdUMP**, binds to TS forming an unstable binary complex
- In the presence of folate (**MTHF – arfolitixorin** or leucovorin after conversion), a more stable ternary complex is formed -> provided that MTHF is present from the start



- The ternary complex inhibits TS effectively
>> resulting in interrupted tumor cell DNA synthesis and repair



- Tumor cell death
>> anti-tumor effect (DNA damage and tumor cell apoptosis)

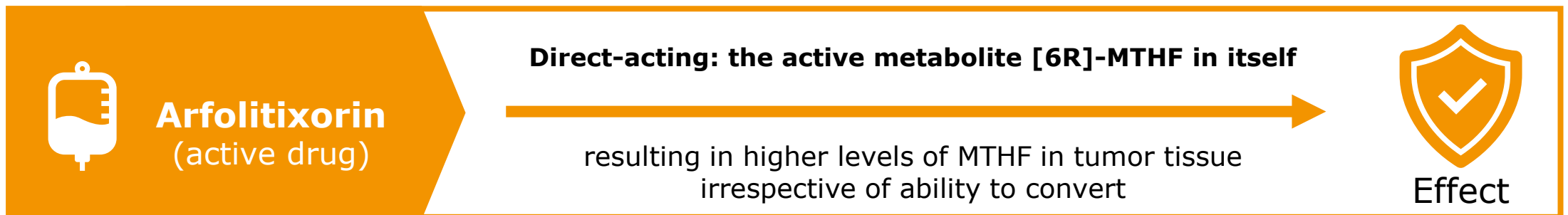
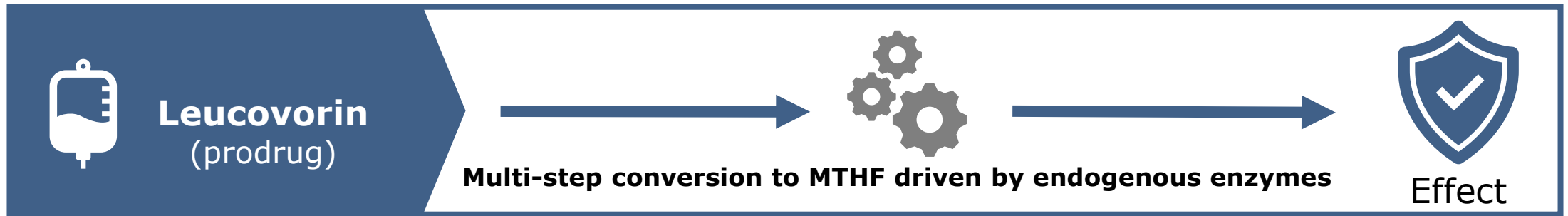
The basis of our value creation

**High medical
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**Arfolitixorin has
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**High market
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Arfolitixorin does not require conversion and metabolization to become active



→ Aim: Improved outcomes (ORR, PFS, OS)

Why did arfolitixorin only indicate similar efficacy as SoC in the phase III trial AGENT? → **Dosing regimen suboptimal**



Low dose

Arfolitixorin was given in <50% lower dose than leucovorin

→ inaccurate comparison between arms



Wrong timing

Arfolitixorin was given 30 min *after* 5-FU bolus, in contrast to leucovorin that was given *before* which is clinical practice

→ risk that the TS+FdUMP complex formation, which starts swiftly following 5-FU administration, had already begun when arfolitixorin was given → only the instable, binary complex formed



Too little, too late:

less TS inhibition and lower anti-tumor effect

Now conducting a new clinical phase Ib/II-study with an optimized dosing regimen

Treatment-naïve patients with metastatic colorectal cancer.

Arfolitixorin replacing leucovorin in combination with 5-FU based chemotherapy.

Optimized dose and administration based on previously generated data.

Strategic development collaboration with one of the world's leading hospitals



**Prof. Dr. med.
Sebastian Stintzing**

Head of the Department of
Hematology, Oncology and
Cancer Immunology (CCM)

Principal investigator



Isofol's collaboration with global top experts reinforces the viability of the clinical program



Sebastian Stintzing



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Comprehensive dataset de-risks the continued clinical program

ISO-CC-002 (Phase I/II)

ISO-CC-005 (Phase I/II)

The AGENT study (Phase III)

Post hoc-analysis of the AGENT study

Tumor homogenate studies

Cell line experiments

Tumoroid studies

Tissue-level study

Comprehensive dataset de-risks the continued clinical program (1/3)

ISO-CC-002 (Phase I/II)

ISO-CC-005 (Phase I/II)

The AGENT study (Phase III)

Post hoc-analysis of the AGENT study

Tumor homogenate studies

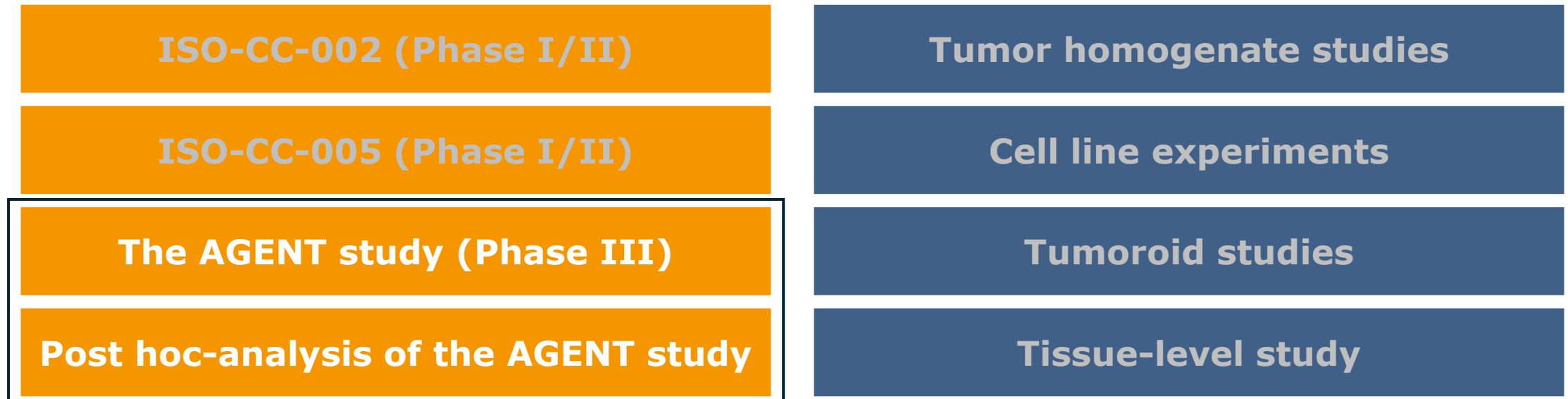
Cell line experiments

Tumoroid studies

Modelle study

▶ Phase I/II-studies indicate that the drug candidate is safe, well tolerated and show efficacy.

Comprehensive dataset de-risks the continued clinical program (2/3)



- ▶ Global, randomized phase III-study did not meet endpoint of superiority but showed that the drug is active (comparable efficacy to leucovorin in the ITT population with the chosen dosing regimen)
- Post-hoc, per-protocol analysis indicates possible superior efficacy

Analyses identify the main reasons for the AGENT trial outcome: suboptimal dosing regimen



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Too little, too late:

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Comprehensive dataset de-risks the continued clinical program (3/3)

ISO-CC-002 (Phase I/II)

ISO-CC-005 (Phase I/II)

The AGENT study (Phase III)

Post hoc-analysis of the AGENT study

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Cell line experiments

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Tissue-level study

- ▶ Recent studies strengthen the evidence further and underpins the restart of the clinical program, e.g. by pointing at a strong **dose-response relationship** (higher doses of arfolitixorin gives higher efficacy, in contrast to leucovorin).

Stable evidence platform for the continued development

1

Arfolitixorin has already shown efficacy in an extensive Phase 3 study with a suboptimal dosing regimen.



2

Higher doses given earlier in time is expected to lead to better efficacy.



3

Higher doses can most likely be given without affecting the safety profile as doses in that range has been tested successfully before.*



*) Studies have been conducted with doses up to 500 mg/m² (in healthy volunteers) and 240 mg/m² (in patients with metastatic colorectal cancer in combination with 5-FU and other drugs) with a maintained safety profile.



All findings are integrated in the design of the new study

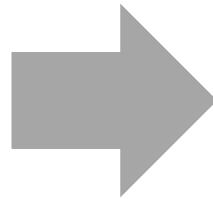
Phase Ib/II study:

- **Higher dose** → higher efficacy.
- **Earlier start, extended administration time** → optimizing conditions for synergistic interaction with 5-FU and effective TS inhibition, ensures safety

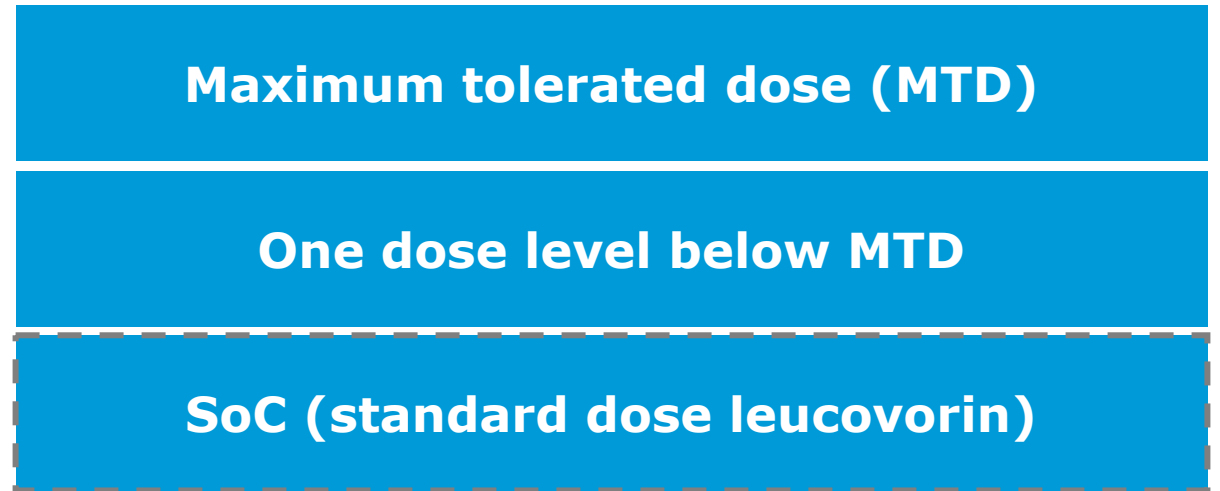
Study design

Phase 1b:
Dose escalation (<20 patients)

Five dose levels
up to 500 mg/m²
Intravenous short infusion
(up to 20 patients)



Phase 2 (randomized):
Dose optimization (~60 patients)



Preliminary design, not decided

The basis of our value creation

**The unmet
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**High market
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The market for treatment of metastatic colorectal cancer

6

billion USD

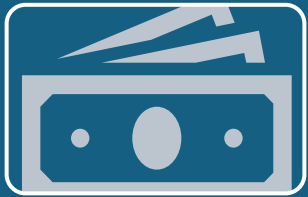
Current market size for
pharmaceutical treatments

7.3

billion USD

Expected market size in
2032

Blockbuster potential in lead indication in the U.S. alone, additional opportunities to add



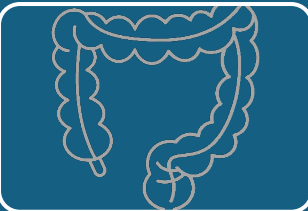
Blockbuster opportunity

- Sales potential exceeding **USD 1 bn** per year at peak) in mCRC in the U.S. alone*
- 60000-70000 addressable patients, significant price premium
- Possible substance patent protection until 2044 (based on a preliminary official patentability report)



Additional markets ex-U.S to be added

- Japan** (Investments from Solasia Pharma K.K.), Canada**
- Europe and all additional regions



Potential additional indications

- In colorectal cancer: Adjuvant / neoadjuvant treatment
- Other forms of solid tumors where 5-FU is used (pancreatic, gastric, breast, head/neck...)

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The Isofol opportunity in short:



Focusing on areas in oncology of high medical need



The amount of data available de-risks the clinical program, efficacy already demonstrated. All CMC in place.



A next-gen version of an established mechanism of action with widespread clinical use: facilitates market adoption



Blockbuster potential revenues, favorable competitive landscape and strong IP protection



Strong team in place to drive flawless and swift execution

Our goal:

To improve the prognosis for millions of cancer patients and thereby create significant value for patients and their families, shareholders and society at large.