

# CANIFITE

**BioPharma Ltd**

**Small Molecules for Big Clinical Needs™**

## Company Presentation

April 2024

NYSE American: CANF

# Forward Looking Statement

This presentation contains forward-looking statements, about Can-Fite's expectations, beliefs or intentions regarding, among other things, its product development efforts, business, financial condition, results of operations, strategies or prospects. All statements in this communication, other than those relating to historical facts, are "forward looking statements". Forward-looking statements can be identified by the use of forward-looking words such as "believe," "expect," "intend," "plan," "may," "should" or "anticipate" or their negatives or other variations of these words or other comparable words or by the fact that these statements do not relate strictly to historical or current matters. Forward-looking statements relate to anticipated or expected events, activities, trends or results as of the date they are made. Because forward-looking statements relate to matters that have not yet occurred, these statements are inherently subject to known and unknown risks, uncertainties and other factors that may cause Can-Fite's actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Important factors that could cause actual results, performance or achievements to differ materially from those anticipated in these forward-looking statements include, among other things, our history of losses and needs for additional capital to fund our operations and our inability to obtain additional capital on acceptable terms, or at all; uncertainties of cash flows and inability to meet working capital needs; the initiation, timing, progress and results of our preclinical studies, clinical trials and other product candidate development efforts; our ability to advance our product candidates into clinical trials or to successfully complete our preclinical studies or clinical trials; our receipt of regulatory approvals for our product candidates, and the timing of other regulatory filings and approvals; the clinical development, commercialization and market acceptance of our product candidates; our ability to establish and maintain strategic partnerships and other corporate collaborations; the implementation of our business model and strategic plans for our business and product candidates; the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and our ability to operate our business without infringing the intellectual property rights of others; competitive companies, technologies and our industry; risks related to the COVID-19 pandemic and the Russian invasion of Ukraine; risks related to not satisfying the continued listing requirements of NYSE American; and statements as to the impact of the political and security situation in Israel on our business. More information on these risks, uncertainties and other factors is included from time to time in the "Risk Factors" section of Can-Fite's Annual Report on Form 20-F filed with the SEC on March 30, 2023 and other public reports filed with the SEC and in its periodic filings with the TASE. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Can-Fite undertakes no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by any applicable securities laws.

# Company Overview

1

**Safe Drugs for the Treatment of  
Oncological and Inflammatory Diseases**

2

**Advanced Clinical Stage  
Pipeline; Short Regulatory  
Approval Pathway (FDA & EMA)**

3

**Successful Out-licensing  
Deals**

4

**Financial Summary**

(Ticker: CANF) Listed on NYSE American and Tel-Aviv Stock Exchange  
~6 M ADRs outstanding; ~1,225 M ordinary shares outstanding  
(1 ADR = 300 Ordinary Shares)  
Cash: \$8.9M as of December 31, 2023

# Unique Platform Technology

Specific oral therapy aimed at diseased cells

## Therapeutic Target

- Global leader in discovering and developing drugs that target the A3 adenosine receptor (A3AR)

## Pipeline Drugs

- Small molecule, orally bioavailable drugs
- Bind only to pathological cells, not normal cells

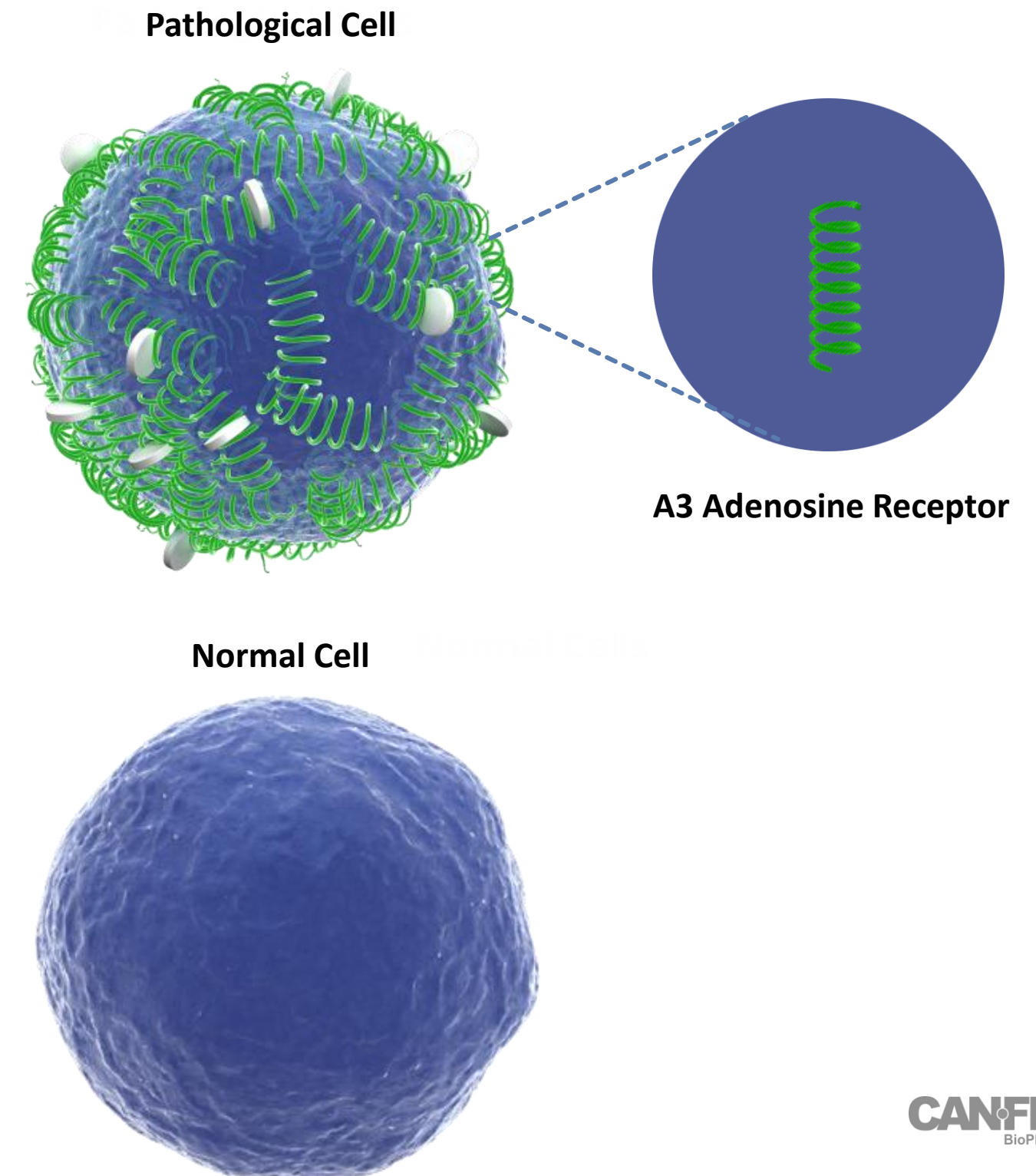
## Proven Therapeutic Effect

- High efficacy and good safety with anti-inflammatory and anti-cancer effects shown in Phase 2 and Phase 3 studies

## Excellent Safety Profile

- Demonstrated in >1600 patients







NYSE: CANF



# Pipeline Drugs

Drug/Indication	Pre-Clinical	Phase 1	Phase 2	Phase 3
<b>Piclidenoson</b> Psoriasis	Pivotal Phase III agreed with FDA & EMA			
<b>Namodenoson</b> Liver Cancer	Pivotal Phase III agreed with FDA & EMA Ongoing			
Pancreatic Cancer	Phase IIa to be initiated Q2			
MASH (NASH)	Phase IIb Ongoing			
<b>CF602</b> Erectile Dysfunction	Ongoing			
<b>Cannabinoids</b>	Ongoing			

# Corporate Partnerships: Current Out-Licensing Deals

	<b>Eastern Europe</b>	<i>Psoriasis, Liver Cancer, MASH Pancreatic cancer</i>
	<b>Spain, Switzerland, Austria</b>	<i>Psoriasis</i>
	<b>China, Taiwan, Hong Kong, Macao</b>	<i>Psoriasis, Liver Cancer, MASH</i>
	<b>South Korea</b>	<i>Liver Cancer, MASH</i>
	<b>South Korea</b>	<i>Psoriasis</i>
	<b>Canada</b>	<i>Psoriasis</i>
<b>VETBIOLIX</b>	<b>Global</b>	<i>Piclidenoson - Pets' Osteoarthritis</i>

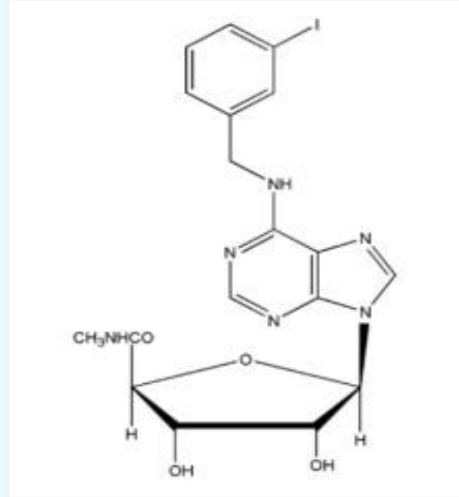
**\$20M** received in upfront and milestone payments

**\$130M** potential based on regulatory and sales milestones

**Typical Deal Structure**

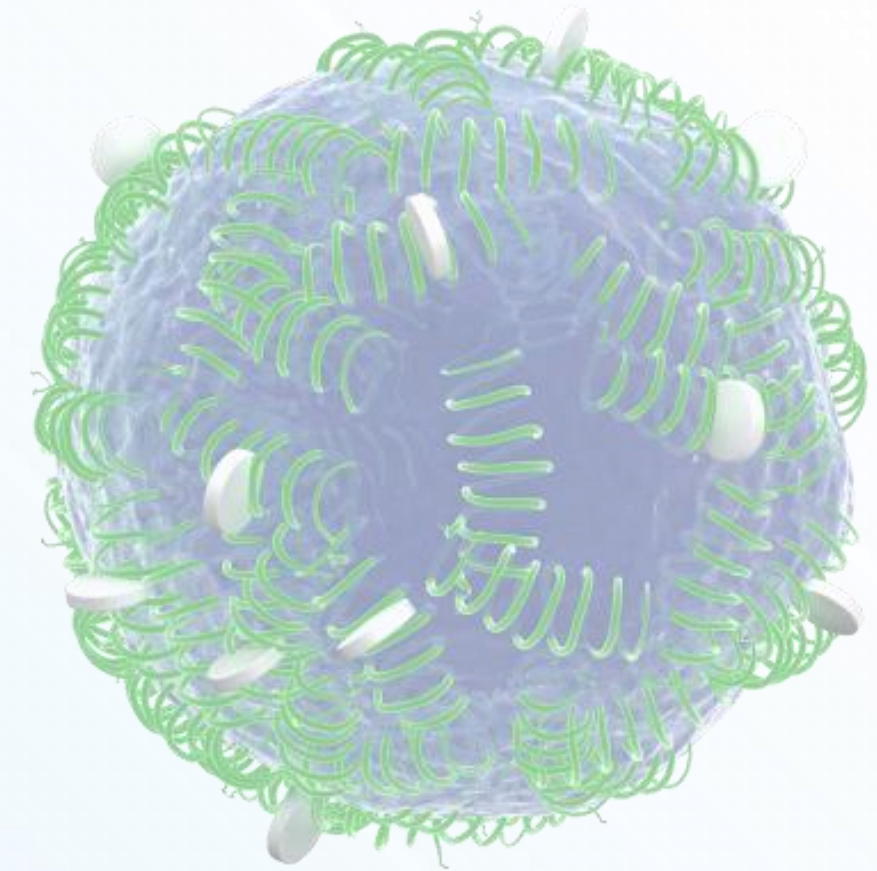
- Up-front money upon signing a distribution deal
- Regulatory milestone payments
- Royalties (double-digits)
- Sales milestone payments

## Piclidenoson Drug Candidate



### Chemical Properties

- Nucleoside derivative
- Highly Selective A3AR Agonist
- Molecular weight - 510.29
- Water insoluble
- Half lifetime in blood – 8-9 hours

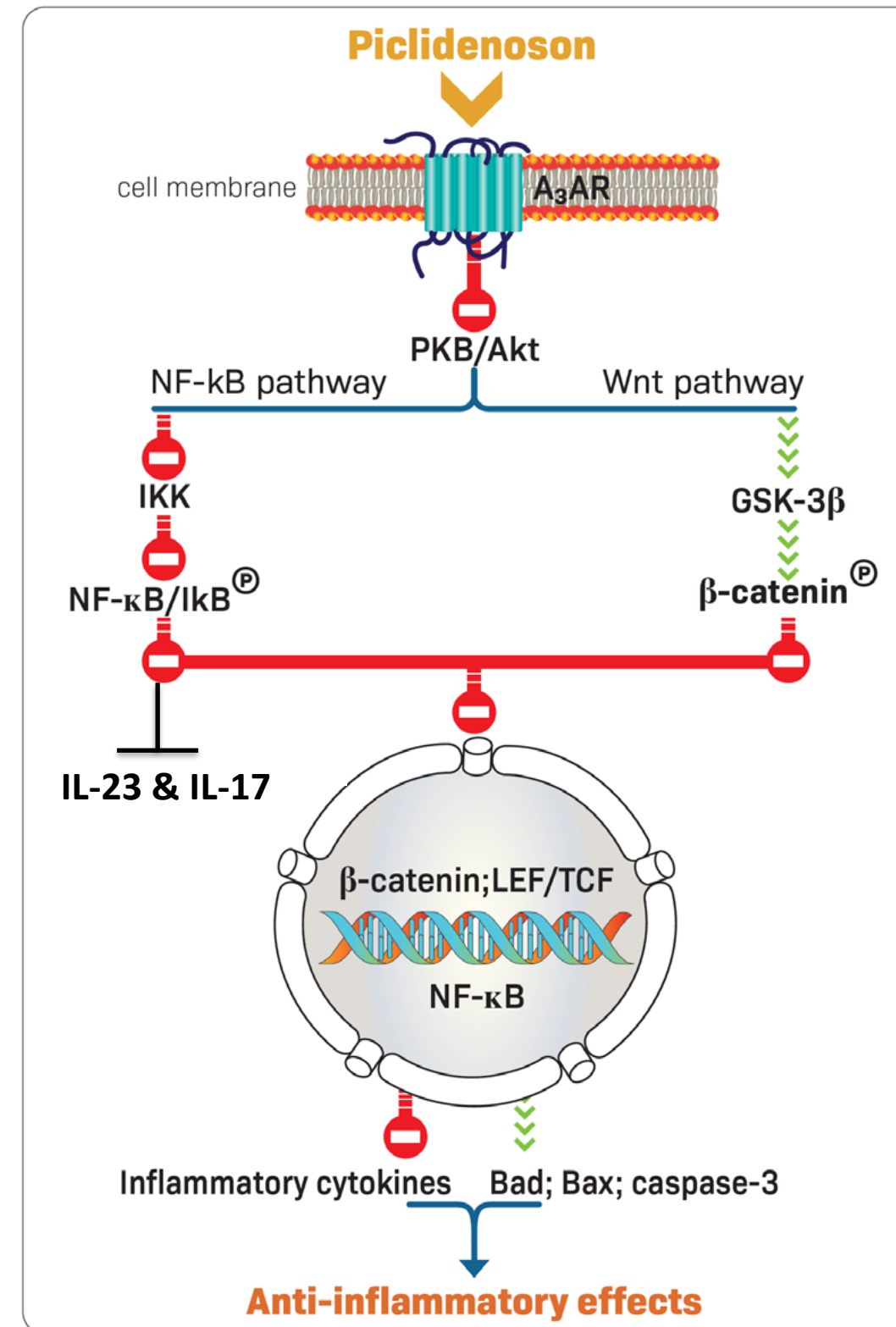


**Piclidenoson**  
Moderate to Severe Psoriasis

# Piclidenoson for the Treatment of Plaque Psoriasis

## Rational for Development

- Overexpression of the A3AR target in Keratinocytes of psoriasis patients
- Robust anti-inflammatory effect manifested by specific apoptosis of inflammatory cells
- Piclidenoson inhibits **IL-17 & IL-23** production in keratinocytes
- Piclidenoson had significant anti-psoriatic effects and promising safety profile in a Phase 3 trial in patients with moderate-to-severe plaque psoriasis.



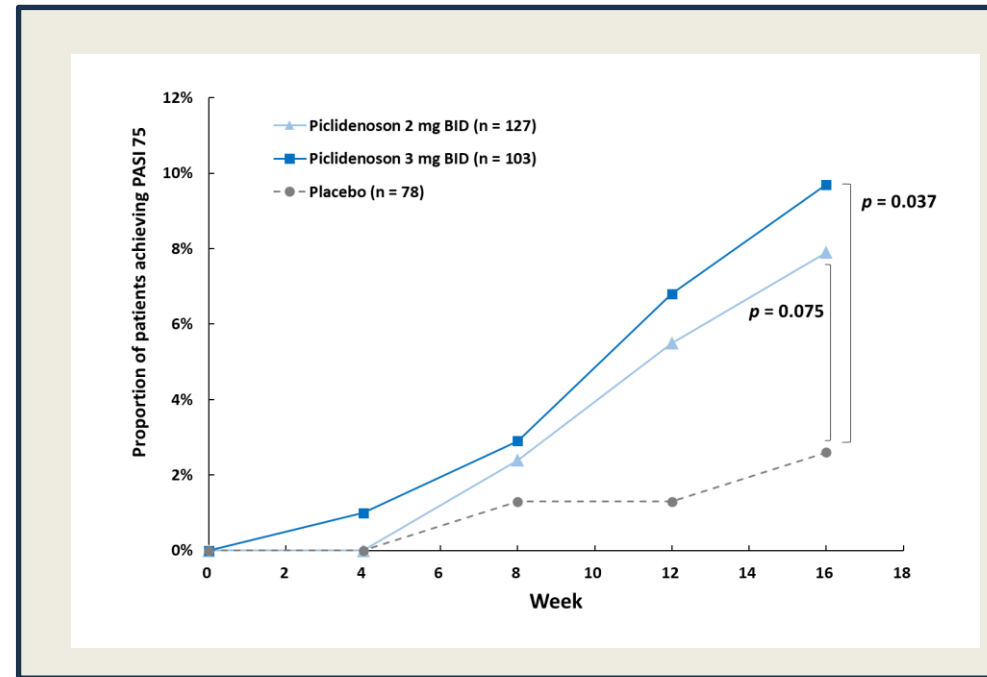


# Phase III Study Endpoints - Achieved



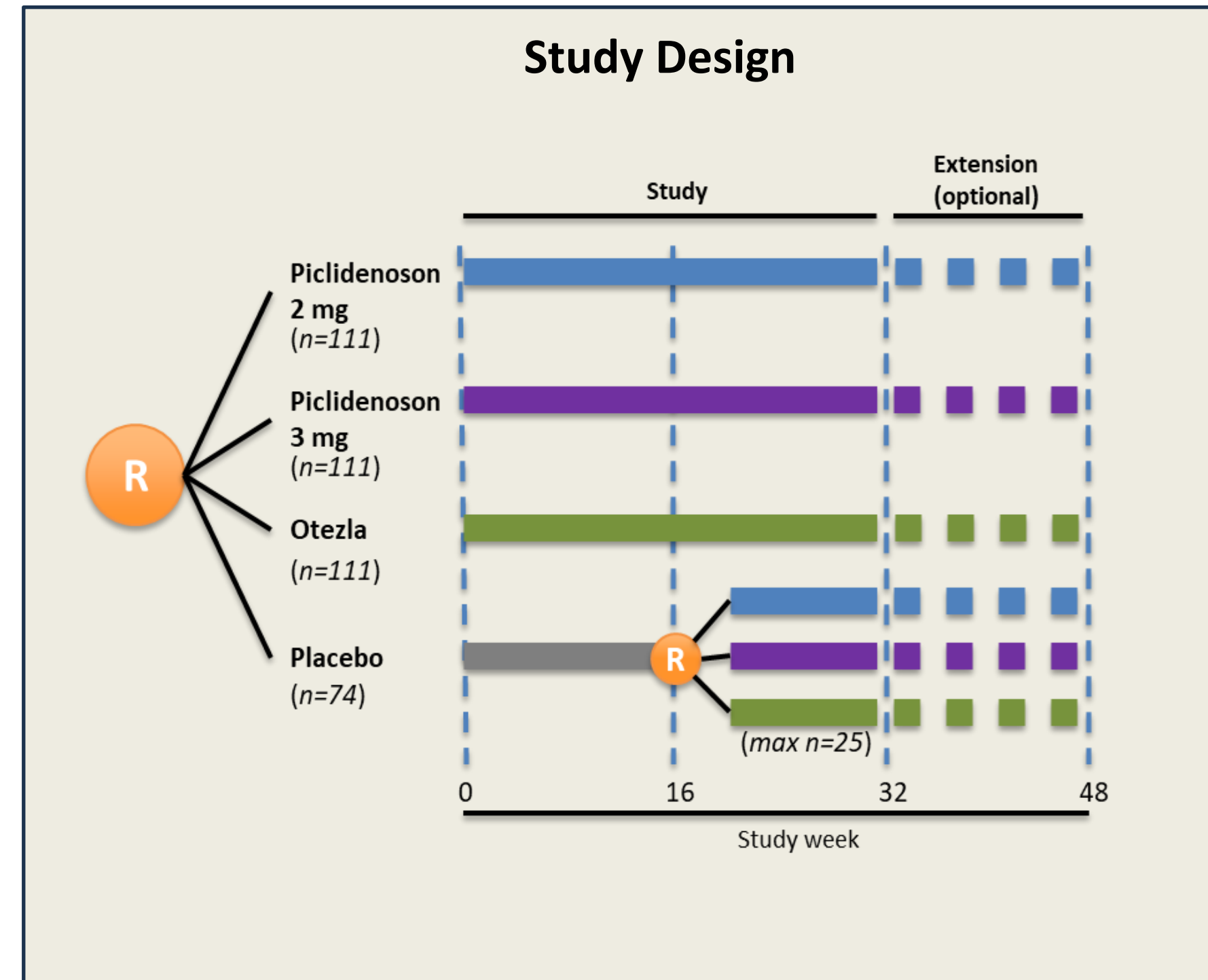
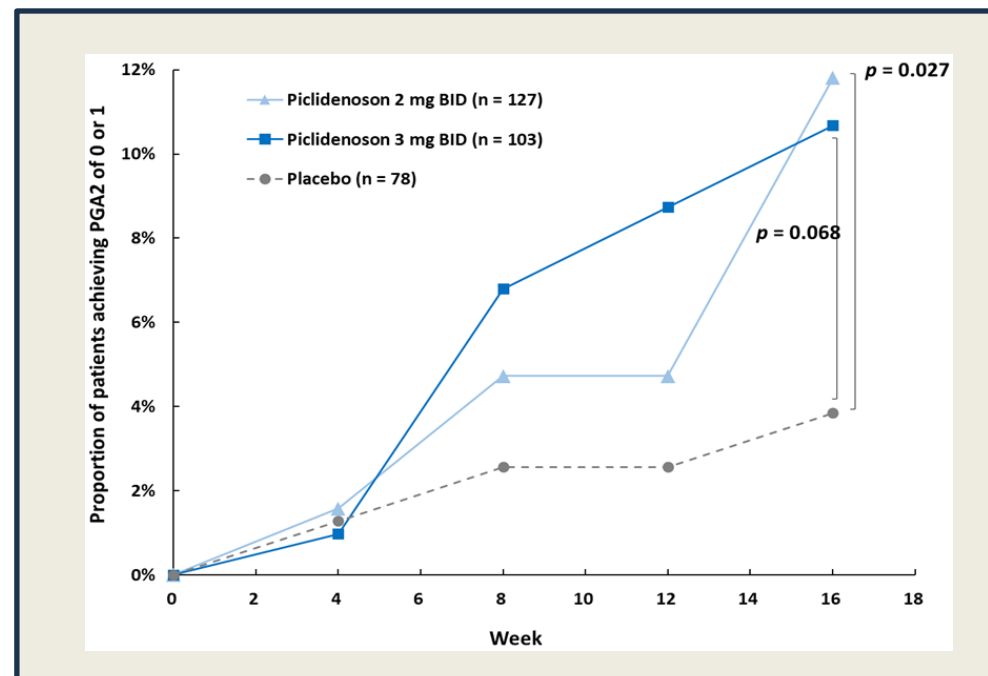
## Primary Endpoint

PASI 75 Significant Superiority of Piclidenoson 3 mg vs. Placebo



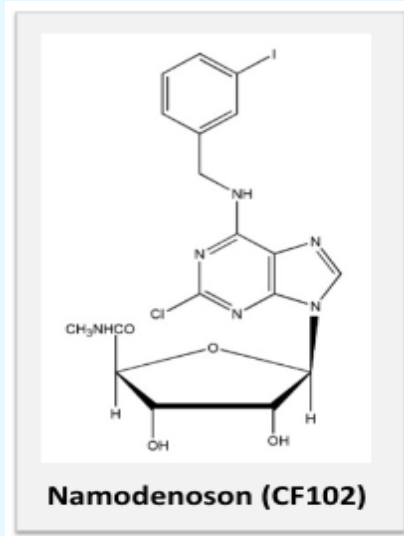
## Secondary Endpoint

Subjects Achieving PGA2 for Piclidenoson vs Placebo



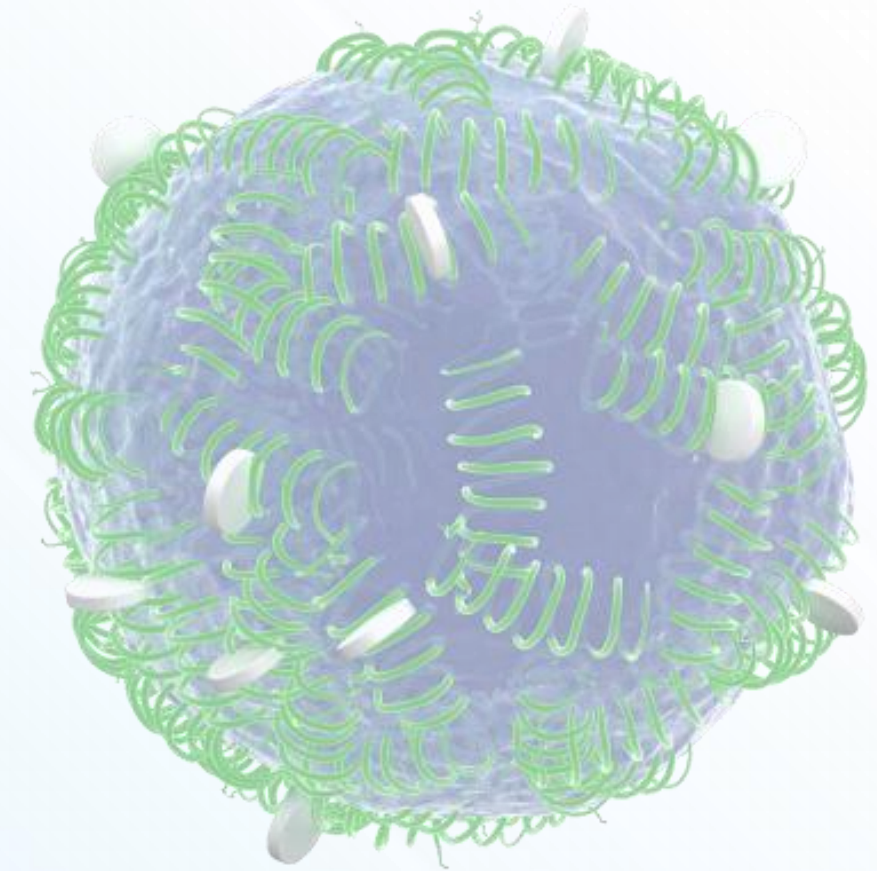
# Excellent Safety Profile

# Namodenoson Drug Candidate



## Chemical Properties

- MW: 544.73 g/mol
- Water Insoluble
- Half life: 12 hours
- Nucleoside Derivative
- Orally Bioavailable
- High Stability in the Liver

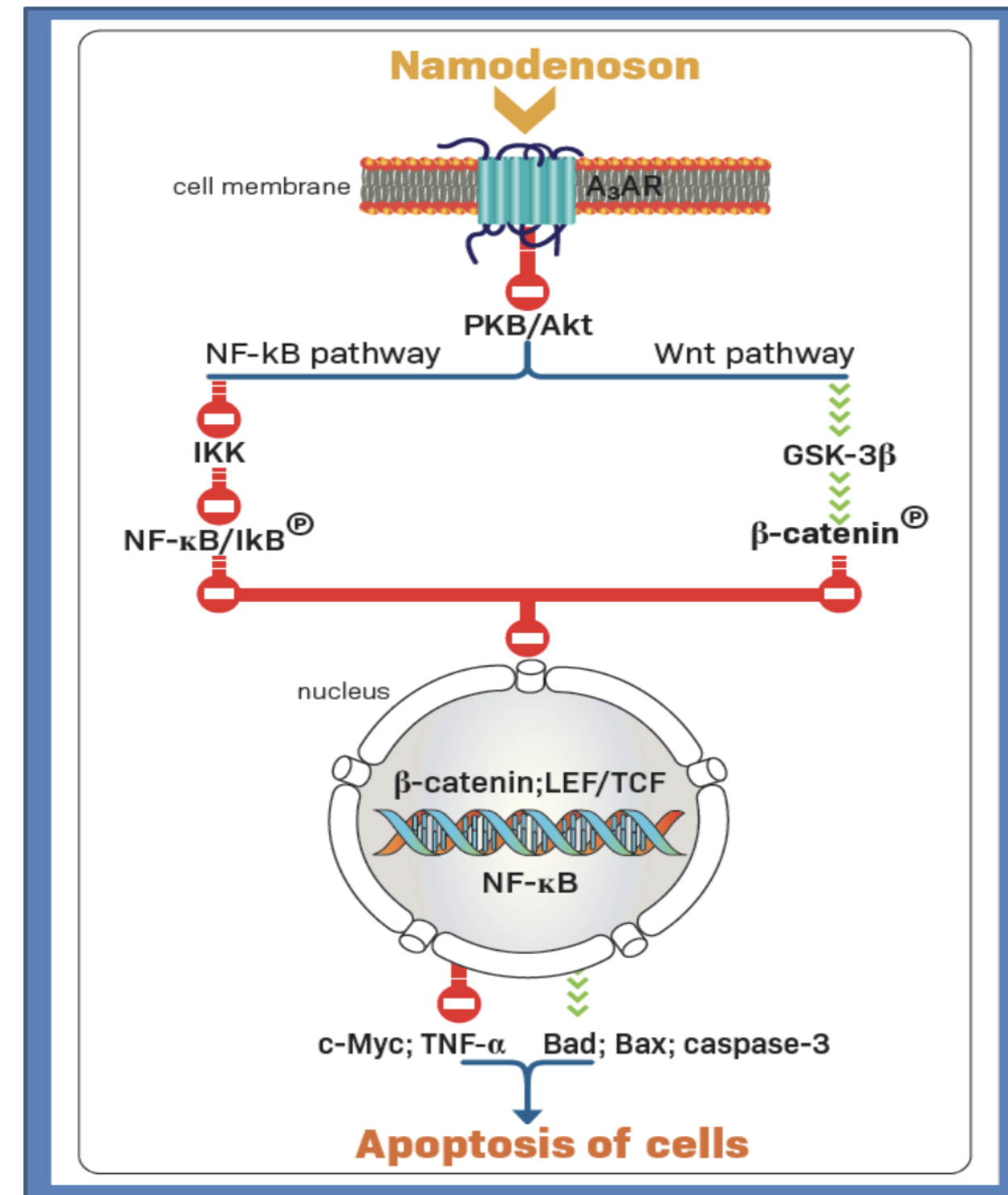


**Namodenoson**  
Oncology & MASH (NASH)

# Advanced Liver Cancer

## Rational for Development

- A3AR is over-expressed in human hepatocellular carcinoma (HCC) cells.
- Namodenoson, induces de-regulation of the Wnt and NF- $\kappa$ B signalling pathways resulting in apoptosis of HCC cells.
- In Phase II study in patients with advanced HCC, namodenoson was safe and well tolerated. Evidence of antitumor activity was observed.



# HCC Phase II Study – Recent Data

## Presented at the AASLD 2022 & ASCO-Breakthrough 2023 Meeting

### Complete Response in a Namodenoson Treated Patient

- Patient was enrolled in Phase II liver cancer study
- Continued treatment with Namodenoson for >6 years under Open Label Extension Program in Europe
- Patient had Complete Response: Completely cleared all cancer lesions
- Over the course of 7 years, clinical benefits included:
  - Disappearance of ascites
  - Return to normal liver function
  - Disappearance of peritoneal carcinomatosis

Complete disappearance  
of tumor lesions



# Liver Cancer

## Pivotal Phase III Ongoing

*Orphan Drug Designation  
with FDA&EMA*

*Fast Track Designation with  
FDA*

*Interim Analysis*

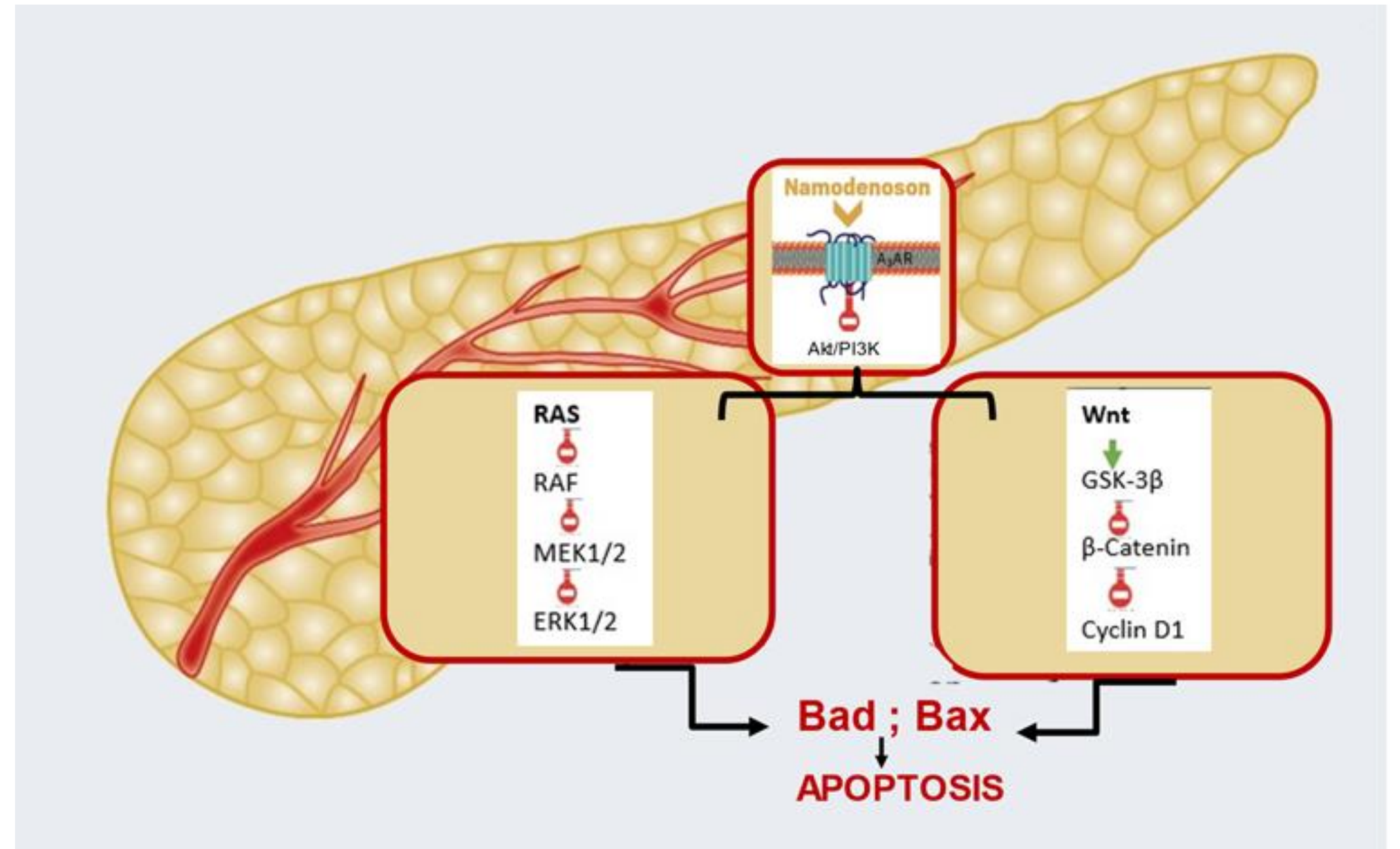
# LIVERATION

- **FDA and EMA** agreed on Pivotal Phase 3 study protocol
- **Interim analysis** to be conducted by Independent Data Monitoring Committee (IDMC) after 50% of planned 450 patients are enrolled and treated
- **Namodenoson evaluated as a 2nd- or 3rd-line** treatment for advanced liver cancer patients in whom other approved therapies have not been or are no longer effective
- **Primary endpoint** - overall survival
- **Orphan Drug Status** - granted by FDA and EMA
- **Fast Track Status** - granted by FDA
- **Compassionate Use Program** - currently treating liver cancer patients in Israel and Romania

# Pancreatic Cancer

## Rational for Development

- Namodenoson induces 90% growth inhibition of pancreatic cancer cells
- The molecular mechanism of action includes de-regulation of the Wnt and the Ras signaling pathways
- *In vivo* studies showed robust inhibition of pancreatic tumor size

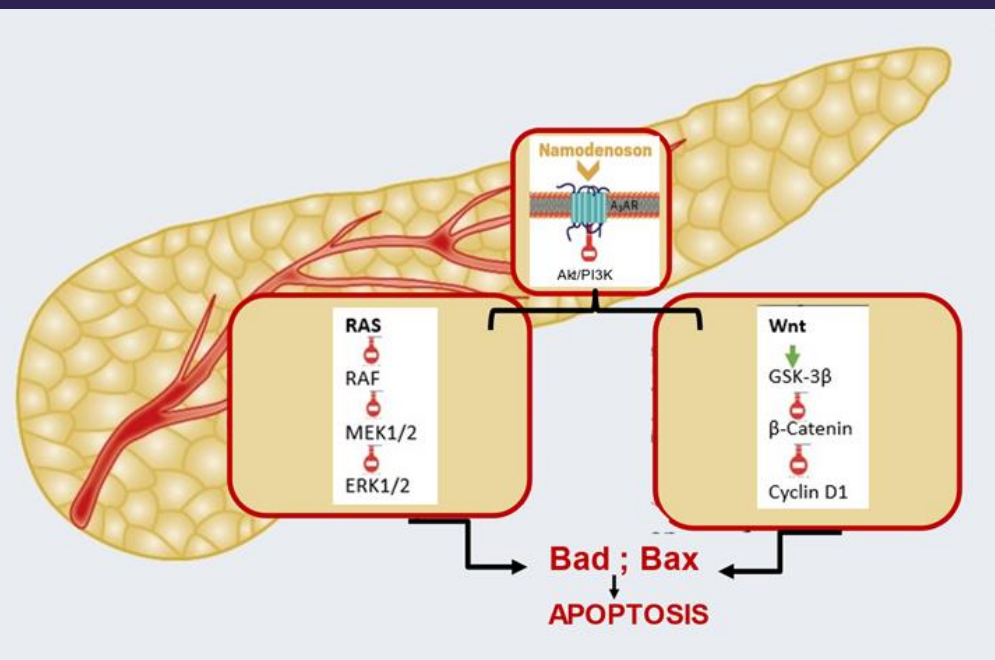


# Pancreatic Cancer

## Exploratory Phase IIa Study – To be initiated Q2 2024

### Second line therapy

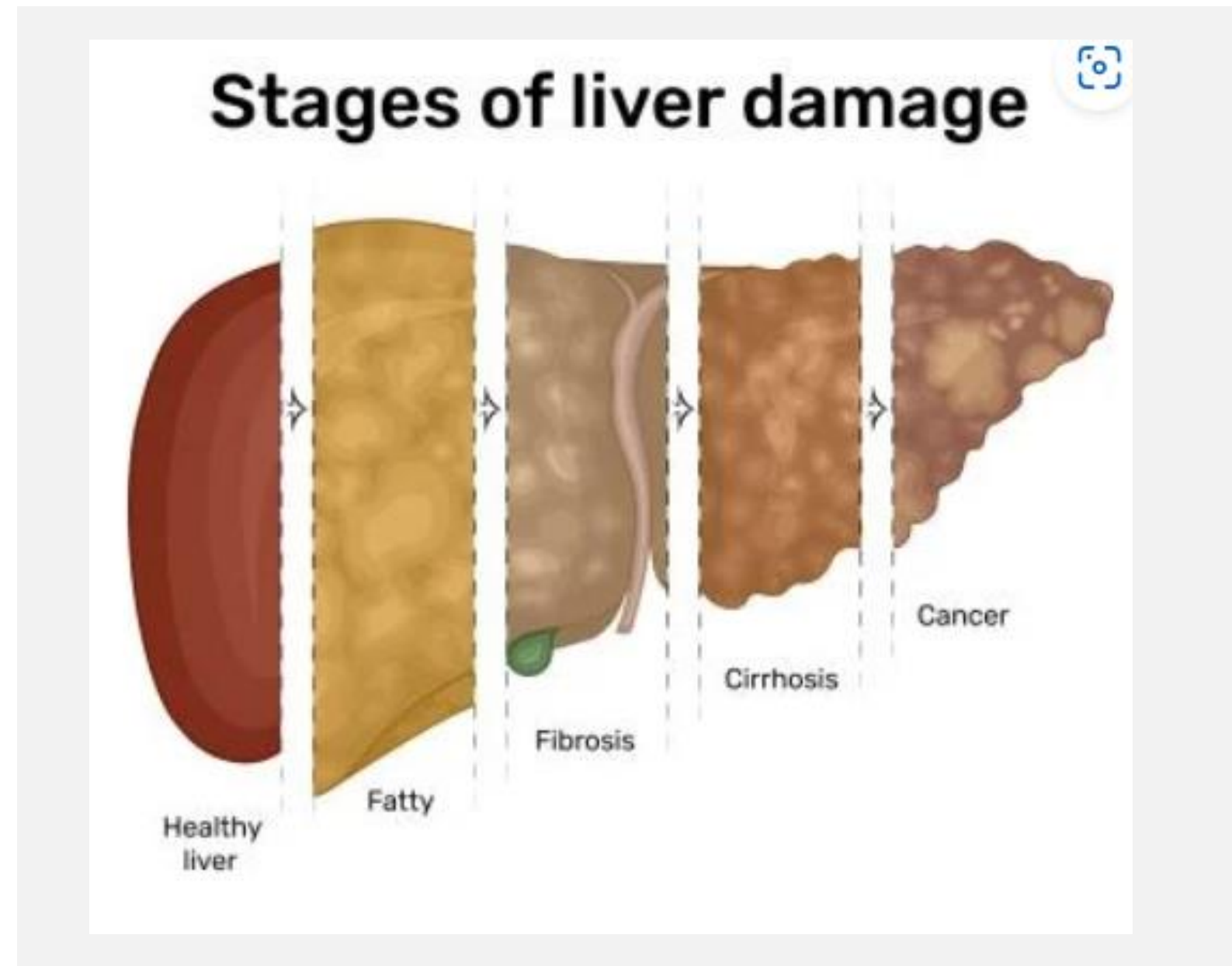
- **Open label**
- **Oral dose of Namodenoson:** 25 mg twice daily
- **Primary End point:** Safety
- **Secondary Endpoints:** objective response, progression-free survival, duration of response, disease control (defined as an objective response or stable disease), overall survival



# MASH - Metabolic Associated Steatohepatitis

## Rational for Development: Liver protective Effect

- Induction of anti - inflammatory effect manifested by reduction of NAFLD Activity Score (NAS)
- Anti-fibrotic effect
- Anti-steatotic effect: significant decrease in steatosis, ballooning and lobular inflammation
- Decrease in ALT, AST, Triglyceride levels
- Namodenoson protects the liver against Ischemia/Reperfusion injury





# MASH

*Addressing Severe Unmet Need*

*Currently Enrolling Patients for a Phase IIb Study*

## Phase IIa Study Successfully Concluded:

- Reduced liver fat content (LFC)
- Anti-Inflammatory effect
- Dose selection for Phase IIb determined
- Decrease in body weight
- Excellent safety

## Phase IIb Study

- Multicenter, randomized, double-blind, placebo-controlled study in 140 subjects with biopsy-confirmed MASH
- Subjects are randomly assigned in a 2:1 ratio to oral doses of Namodenoson 25 mg every 12 hours or a matching placebo for 36 weeks
- Regular evaluation for safety and efficacy biomarkers baseline measurements at weeks 6, 12, 24, and 36
- Primary efficacy endpoint will be determined by liver biopsy at week 36

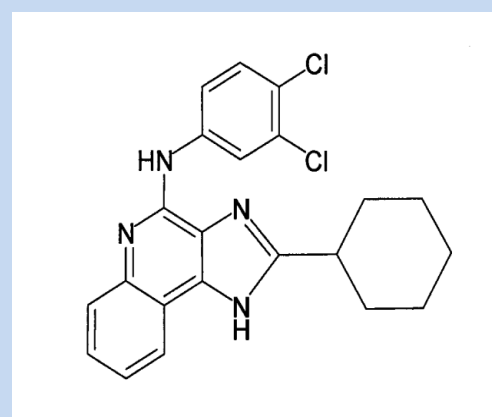
# CF602

## Erectile Dysfunction (ED)

### **Rationale:**

*Anecdotal reports from patients treated with Can-Fite drugs, both women and men, testifying that the drugs reversed their sexual dysfunction*

### Chemical Formula:



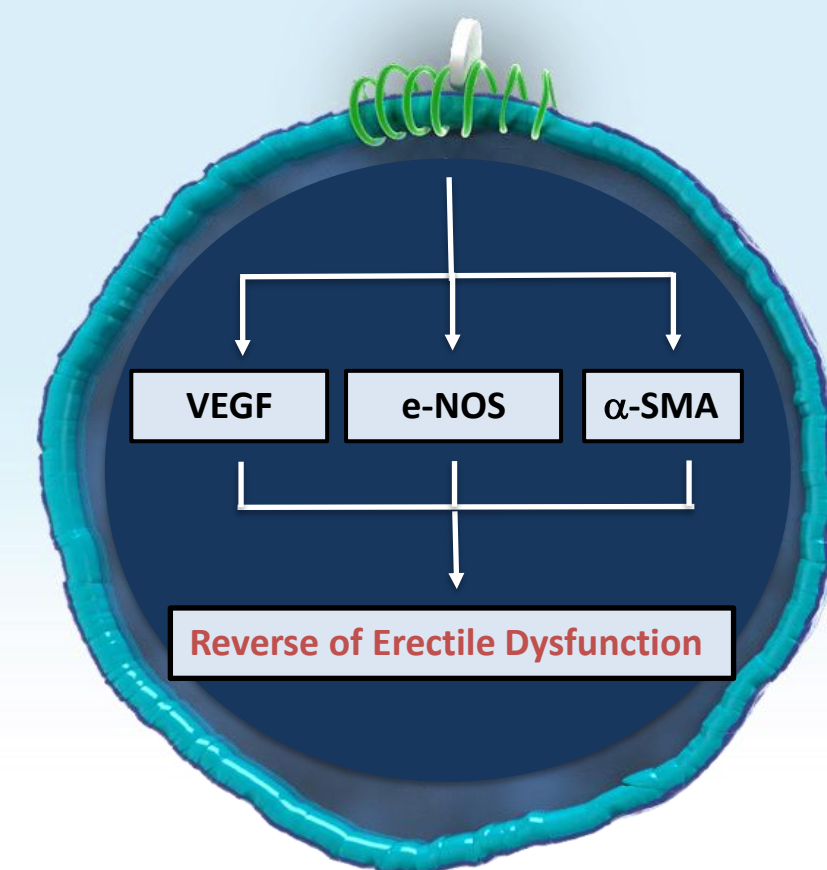
### Properties:

- A3AR allosteric modulator
- Molecular weight – 411.34
- Water insoluble
- Orally bioavailable

### Activity:

- Significant full recovery from erectile dysfunction in a diabetic rat model
- Topically & Systemic
- Dose-dependent, linear effect
- Response after single dose of CF602

### Mechanism of Action



- Up-regulation of eNOS and VEGF
- Improves vasodilation and smooth muscle relaxation

# Cannabinoids

## *Rationale:*

*Cannabinoids are known to bind to A3 adenosine receptor (A3AR) and mediate clinical effects*

## Assay to Identify Clinically Active Cannabinoids

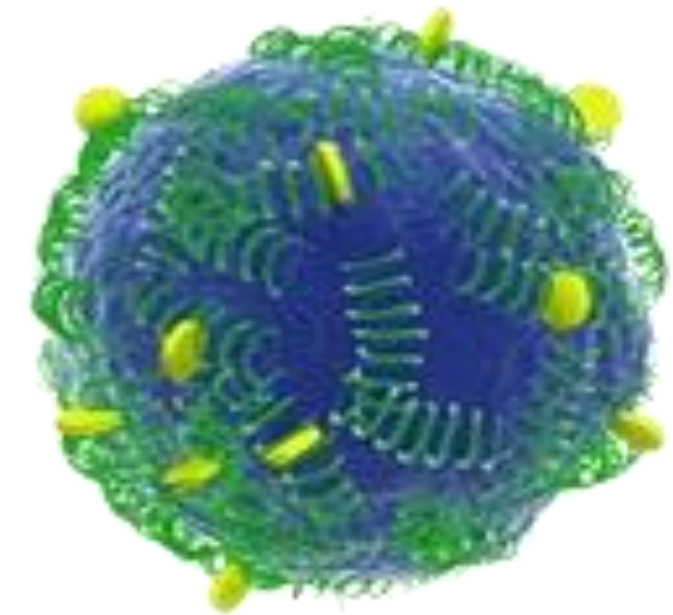
Can-Fite developed a biological assay that identifies clinically active cannabinoids based on the binding to A3AR

## Pre-clinical Data in Liver Cancer and Fibrosis

Based on this assay, Can-Fite has demonstrated how CBD-rich T3/C15 binds to A3AR to inhibit the growth of hepatocellular carcinoma and liver stellate via de-regulation of the Wnt/ $\beta$ -catenin pathway

## Intellectual Property

Can-Fite filed a patent protecting the discovery of cannabinoid-based treatment of diseases where A3AR is overexpressed including liver cancer, other cancers, autoimmune inflammatory and metabolic diseases



 A3AR

 CBD