

# *Kintor Pharma*

*Developing Novel Drugs and Commercialization Platform*

# Accomplishments since 2021



## Out-licensing

Accomplish Kintor's First Sales Revenue **RMB34.23M** in 2021

- Upfront payment of out-licensing contract with Fosun Pharma in India and 28 African countries
- Upfront payment of out-licensing contract with Etana in Indonesia

**FOSUN PHARMA**  
复星医药

**etana**  
Biotech



## Global Innovation

Pioneer of Chinese Innovative Drugs' Globalization

- **3** phase III MRCTs were approved by various countries' administration (FDA included)
- **4** drug candidates (proxalutamide, pyrilutamide, ALK-1 antibody, GT20029) have clinical trials carried out within and out of China.



## Clinical Trial

**10** Clinical Trials Moved to Phase III/II Stage

- **Proxalutamide**  
3 phase III MRCTs for COVID-19
- **Pyrilutamide**  
1 phase III trial for male AGA in China  
1 phase II trial for female AGA in China  
1 phase II trial for male AGA in the U.S.  
1 phase II trial for acne in China
- **ALK-1 antibody**  
1 phase II trial for HCC in the U.S.  
1 combotherapy trial with PD-1 for HCC in China  
1 combotherapy trial with KN046 for various tumors in Taiwan
- **2 Drug Candidates Moved to Clinical Stage**
  - AR-PROTAC compound (GT20029)
  - PD-L1/TGF- $\beta$  dual-target antibody



## Capacity Building

Growing Self-owned Capacity

- Achieved 1M courses/month in proxalutamide and by the end of 2022, and expects **50M courses/year**.
- Suzhou factory passed **QP audit of EU**. Kintor set up tinctures and gels production line, and obtained drug production license.
- Zhuhai office started operating to speed up the R&D, production, and commercialization of biological drugs
- The Pinghu base covers 40,000  $m^2$  and construction will start in Q2 2022.



## Capital Market

Top-up Placement and Heng Seng Composite Index Included

- Completed a top-up placement and raised HK\$1.16 billion (\$150M)
- The stock was included in **HSCI and the HK Stock Connect**



# Outlook for 2022~2023

## Data Release

### Proxalutamide

- The COVID-19 phase III MRCT for outpatient (NCT04870606) will release the final analysis top-line data soon.
- The COVID-19 phase III MRCT for outpatient (NCT04869228) will release its interim analysis data in H2 2022.

### Pyrilutamide

- Phase II data of male AGA in China will be released by the leading PI at a dermatology symposium in June 2022.
- Phase II data of female AGA in China will be released in Q4 2022.

## Clinical Progress

### Pyrilutamide

Patient enrollment will complete for the phase III male AGA and phase II acne clinical trial in China in H1 2022.

### ALK-1 Antibody

Complete FPI of the phase II clinical trial for the second-line combotherapy with Nivolumab for HCC in the U.S. in H1 2022.

### GT20029

Complete all patient enrollment and dosing for phase I clinical trial in China and the U.S. in 2022.

### GT90008

Complete FPI for the phase I clinical trial in China in H2 2022

## NDA/ GMP

### NDA application and commercial production (GMP)

- COVID-19 indication
- AGA indication
- Large scale production of proxalutamide tablets in Suzhou base



\*FPI: first patient in

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Section 1

# Company Overview

# Kintor at a Glance



**2009**

Established as Suzhou Kintor by Dr. Tong and Dr. Guo



**Oncology & AR-Focused<sup>1</sup>**

Focused on oncology AR-related diseases with substantial unmet medical needs



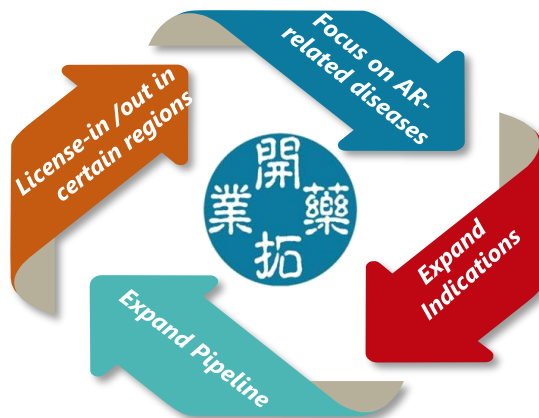
**7+N Pipeline**

Small molecule & biological drugs: 7 potential first/best-in-class in clinical, N in pre-clinical



**Indications**

COVID-19, fastest growing cancers (prostate, breast & liver) globally, and other AR-related indications like AGA<sup>2</sup> and acne vulgaris



**Geographic Expansion**

Potentially leveraging our global relationships to license-out select products for rapid global expansion in the future



**Proxalutamide**

Our lead product, indications in COVID-19, prostate cancer, and breast cancer



**Pyrilutamide**

Indications in androgenetic alopecia and acne vulgaris, phase II trial in China for AGA met primary endpoints, and phase III is ongoing



**ALK-1 antibody**


A new anti-angiogenesis inhibitor, positive data of HCC phase II trial in Taiwan, conducting trials in China and US



Note:

1 AR refers to androgen receptor 2. AGA: androgenetic alopecia

# Products Pipeline

Drug Candidate	Target / Mechanism	Indication	Country/Region	Pre-Clinical	IND Filing (Filed) (Accepted)	Phase I	Phase II	Phase III	NDA
<b>Proxalutamide (GT0918)</b>	Second generation AR antagonist	COVID-19 (Outpatients)	US & Intl		Completed patients enrollment on Dec 23, 2021				
		COVID-19 (Inpatients)	US, China & Intl		Completed FPI on Oct 1, 2021				
		COVID-19 (Outpatients)	China, Brazil & Intl		Completed FPI on Feb 10, 2022 in China				
		mCRPC	China		Expected to submit NDA in 2022				
		Combination therapy with Abiraterone for mCRPC	China		Completed patients enrollment on Feb 24, 2022				
		mCRPC	US		Expected to complete phase II in 2022				
		Metastatic breast cancer	China						
		Combination therapy with Exemestane, Letrozole and Fulvestrant for metastatic breast cancer	China		Completed patients enrollment on Aug 25, 2021				
<b>Pyrilutamide (KX-826)</b>	AR antagonist (for external use)	Androgenetic alopecia (Male)	China		Completed FPI on Dec 31, 2021				
		Androgenetic alopecia (Female)	China		Completed patients enrollment on Mar 4, 2022				
		Androgenetic alopecia (Male)	US		Completed FPI on Feb 28, 2022				
		Acne vulgaris	China		Completed FPI of phase II on Jan 24, 2022				
		Acne vulgaris	US						
<b>ALK-1 (GT90001)</b>	Angiogenesis inhibitor	Combination therapy with a PD-1 for metastatic HCC (2L)	Taiwan		Interim data was released at ASCO GI in Jan 2021				
		Combination therapy with a PD-1 for metastatic HCC (2L)	US & Intl		IND was cleared on Feb 18, 2021				
		Combination therapy with a PD-1 for metastatic HCC	China		IND was approved on Oct 11, 2021				
		Combination therapy with KN046 (PD-L1/CTLA-4) for HCC, GC, GEJ adenocarcinoma, UC, ESCC	Taiwan		Completed FPI on Nov 2, 2021				
<b>GT20029</b>	AR-PROTAC compound	AGA and acne vulgaris	China		First batch of subjects were dosed on Jul 28, 2021				
		AGA and acne vulgaris	US		First subject was dosed on Feb 1, 2022				
<b>GT90008</b>	PD-L1 / TGF-β dual targeting antibody	Multiple types of solid tumours	China		IND was approved on Oct 21, 2021				
<b>Detorsertib (GT0486)</b>	mTOR kinase inhibitor	Metastatic solid tumours	China		Completed FPI on Feb 18, 2021				
<b>GT1708F</b>	Hedgehog/SMO inhibitor	Blood Cancer	China						
		Basal-cell carcinoma	US						
<b>Pre-Clinical</b>	Other AR-PROTAC compounds	Multiple indications							
	c-Myc inhibitor	Blood cancer							
	ALK-1/VEGF bispecific antibody	Solid tumours							

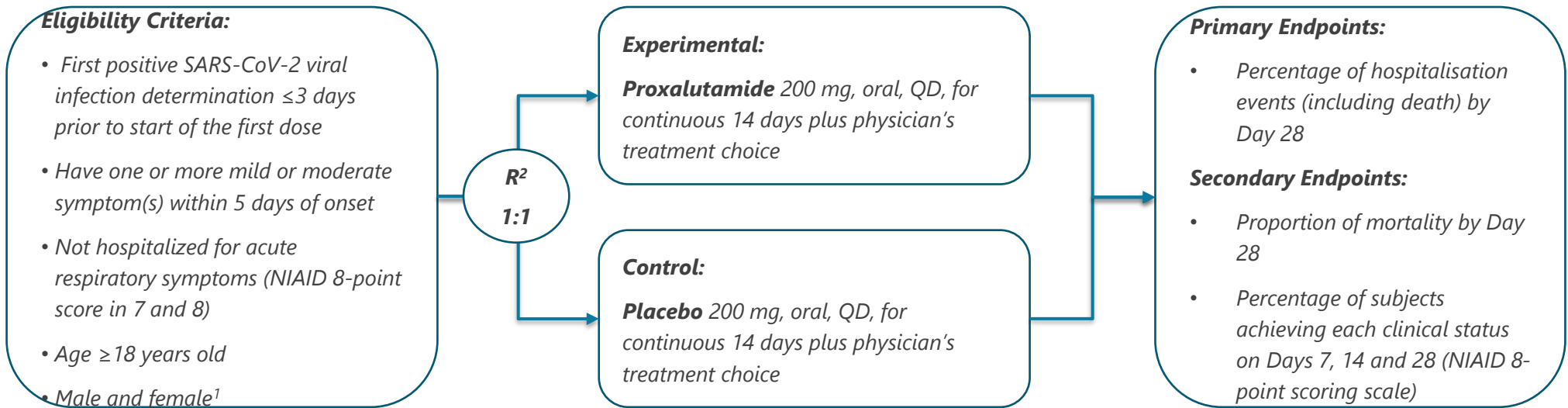
■ Trials initiated by Kintor ■ Trials initiated by Kintor and partners

FPI= First patient in, HCC = hepatocellular carcinoma, GC = gastric carcinoma, GEJ = gastroesophageal junction, UC= urothelial carcinoma, ESCC = esophageal squamous cell carcinoma



# The US & Intl Phase III Study for Outpatients

## The Phase III Study Design (NCT04870606) *Sample Size: 736*



### Countries and regions:

The United States, South America, EU, India, etc.

FDA greenlighted to conduct on Mar 4, 2021

Commenced patients enrolment on April 24, 2021

IND was approved by ANVISA on Jul 19, 2021 in Brazil

Announced interim analysis on Dec 27, 2021



- **Statistical criteria were not met** in interim analysis
- **Good safety profile** and no drug-related SAE
- Expect to lock database in Q1 and will release Top-line data very soon

\*NIAID 8-point scoring scale: By National Institute of Allergy and Infectious Diseases, 1) Death; 2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 4) Hospitalized, requiring supplemental oxygen; 5) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise); 6) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7) Not hospitalized, limitation on activities and/or requiring home oxygen; 8) Not hospitalized, no limitations on activities.



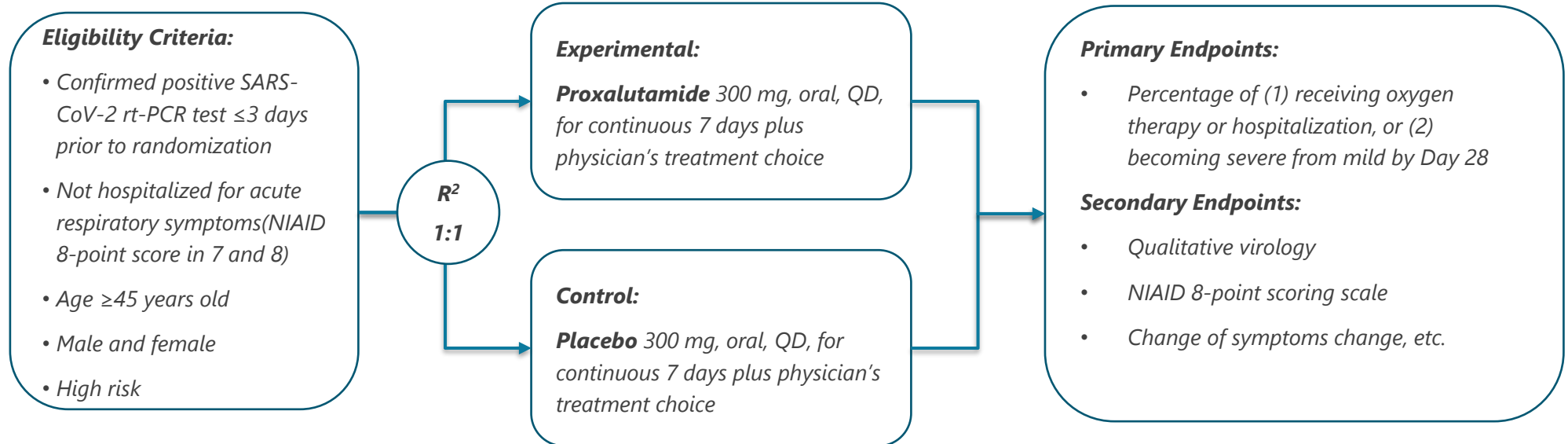
Note: 1. FDA agreed to include female patients on May 17, 2021



# The China, Brazil & Intl Phase III Study for Outpatients

## The Phase III Study Design (NCT04869228)

Sample Size: 724



### Countries and regions:

China, South America (including Brazil), SEA (including Philippines), EU, etc.

IND was approved by ANVISA on Jun 11, 2021 in Brazil

IND approved in Philippines, Malaysia, etc. since Jun

Commenced patients enrolment in Brazil on Aug 4, 2021

IND was approved by NMPA on Sep 1, 2021 in China

FPI in China in Shenzhen 3<sup>rd</sup> People's Hospital on Feb 10, 2022

# The US, China & Intl Phase III Study for Inpatients

## The Phase III Study Design (NCT05009732) *Sample Size: 762*

### Eligibility Criteria:

- PCR positive in sample collected < 72 hours prior to randomization; or PCR positive in sample collected ≥ 72 hours prior to randomization, documented inability to obtain a repeat sample (due to lack of testing supplies, etc.) and progressive disease suggestive of ongoing SARS-CoV-2 infection
- Admitted to a hospital with symptoms suggestive of COVID-19 (NIAID 8-point score in 3 to 5)
- Age ≥ 18 years old
- Male and non-pregnant female

R<sup>2</sup>  
1:1

### Experimental:

**Proxalutamide** 300 mg, oral, QD, for continuous 7-14 days plus physician's treatment choice

### Control:

**Placebo** 300 mg, oral, QD, for continuous 7-14 days plus physician's treatment choice

### Primary Endpoints:

- The need for intensive care unit (ICU) admission or invasive mechanical ventilation/ECMO or all-cause mortality within 30 days of randomisation

### Secondary Endpoints:

- The time to sustained recovery\* evaluated by Day 30
- Safety, etc.

### Countries and regions:

The United States, China, South America, EU, India, etc.

FDA greenlighted to conduct on May 17, 2021

IND was approved by NMPA on Sep 1, 2021 in China

IND was approved by ANVISA on Sep 26, 2021 in Brazil

Commenced patients enrolment on Oct 1, 2021 in US

\*Day of sustained recovery is defined as the first day on which the subject satisfies one of the following three categories from the NIAID ordinal scale and maintains a score of 6, 7 or 8 through Day 30. (6) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; (7) Not hospitalized, limitation on activities and/or requiring home oxygen; (8) Not hospitalized, no limitations on activities.





Section 2

# Introduction of Candidates in Clinical Stage

# Risk-balanced Pipeline of Potential First- and Best-In-Class

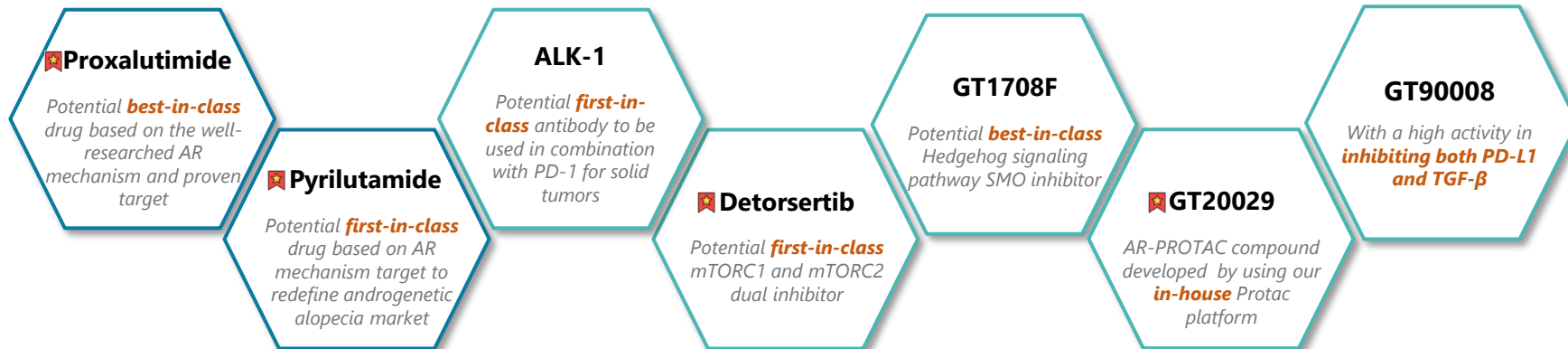
## 1 Products



*Seek incremental yet significant improvements to existing treatment options*



*Innovative drugs that seek to substantially expand the addressable market for the target indications*



**7** clinical-stage candidates

**~20** ongoing clinical studies

**Global clinical program**

in China(including Taiwan), U.S., and Brazil

**Fully in-house**

developed novel compounds

*Proxalutamide - Patent expiration date is Mar 8, 2032; Pyrilotamide - Patent expiration date is Sep 8, 2030*

**Kintor has designed a two-pronged strategy for its Risk-balanced and Diversified product pipeline**

Source: Company Prospectus, Frost & Sullivan analysis





## 2 Summary: MOA of Proxalutamide for COVID-19

### Mechanism 1:

#### **Mechanism of Inhibiting SARS-Cov-2 Entry into the Host Cells**

- a) Proxalutamide inhibited SARS-CoV-2 infection for **WA1 original strain, Alpha and Delta variants** in LNCaP by down-regulating the expression of TMPRSS2 and ACE2.
- b) Proxalutamide inhibited SARS-CoV-2 infection for **SARS-CoV-2 Gamma variant** in humans.

### Mechanism 2:

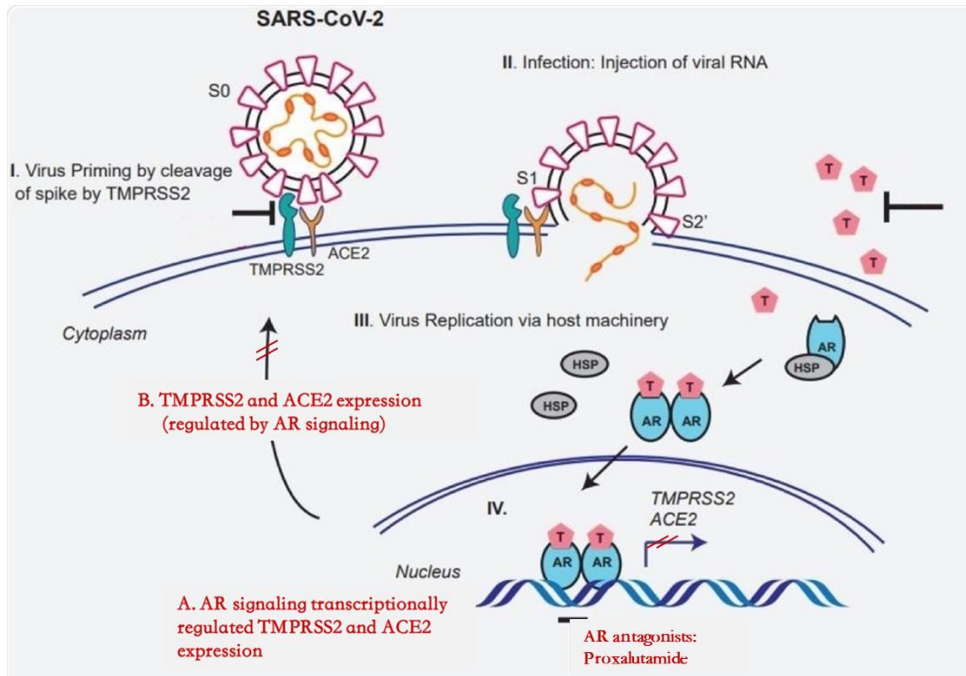
#### **Evidence of Proxalutamide's Impact on Immunity and Inflammation Regulation for COVID-19**

- a) Proxalutamide increased the expression and the activity of **Nrf2**, with potential to counteract symptoms induced by the **cytokine storm** in COVID-19.
- b) Proxalutamide regulated **inflammation related pathway** in RAW264.7 Cells.
- c) Proxalutamide down-regulated **IκBα** phosphorylation and attenuated **NF-κB** signaling.
- d) Proxalutamide down-regulated **iNOS** expression in macrophage cells.
- e) Proxalutamide dose-dependently inhibited LPS-induced **TNF-α** and **IL-6** expression in vitro.
- f) Proxalutamide showed promising signaling in preventing **cytokine storm-induced cell death** in vitro and in vivo.
- g) Proxalutamide inhibited **acute immune response** in Poly I:C-induced acute lung injury animal model (in vivo), and improved **Lung Injury in Hospitalized COVID-19** Patients.



# MoA of Proxalutamide (1) : AR Signaling Regulates

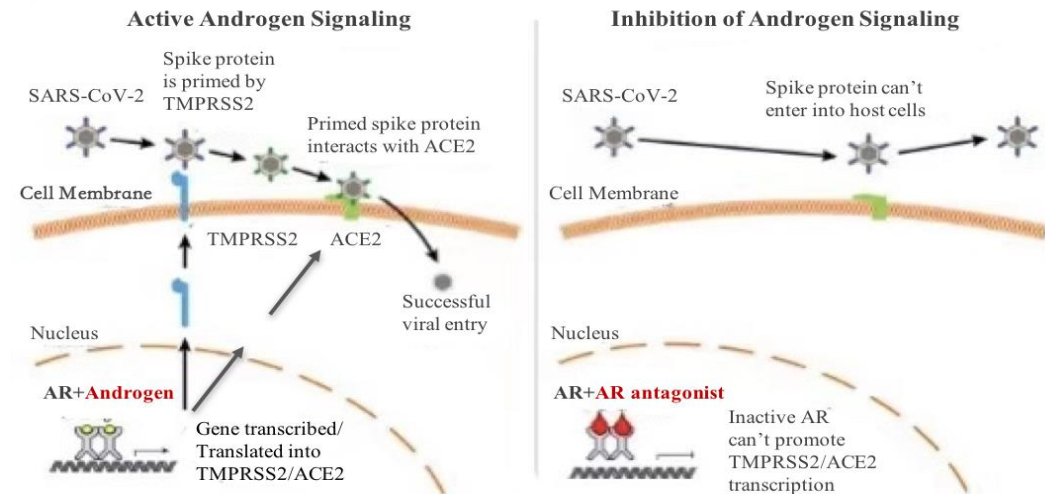
## 2 ACE2/TMPRSS2 Mediated SARS-CoV-2 Infection



**SARS-CoV-2 entry into host cells requires two host cell surface proteins: ACE2 and TMPRSS2.**

- The spike protein need to be primed by TMPRSS2 before it could interact with ACE2 to get the RNA of the virus entered into host cells.
- The expression of TMPRSS2 and ACE2 are positively regulated by the AR signaling.
- Targeting AR-ACE2/TMPRSS2 signal axis could originally inhibit the entry of the virus into host cells by transcriptionally downregulating the expression of TMPRSS2 and ACE2, which has gradually been receiving growing attention as potential therapies for COVID-19.

**AR antagonists (like proxalutamide) inhibit SARS-CoV-2 entry into host cells by inhibiting the function of AR and downregulating the expression of ACE2 and TMPRSS2**



Source: Qiao Y., et al, Proceedings of the National Academy of Sciences. 2021; Leach D. A., et al, Research Square. r2021.

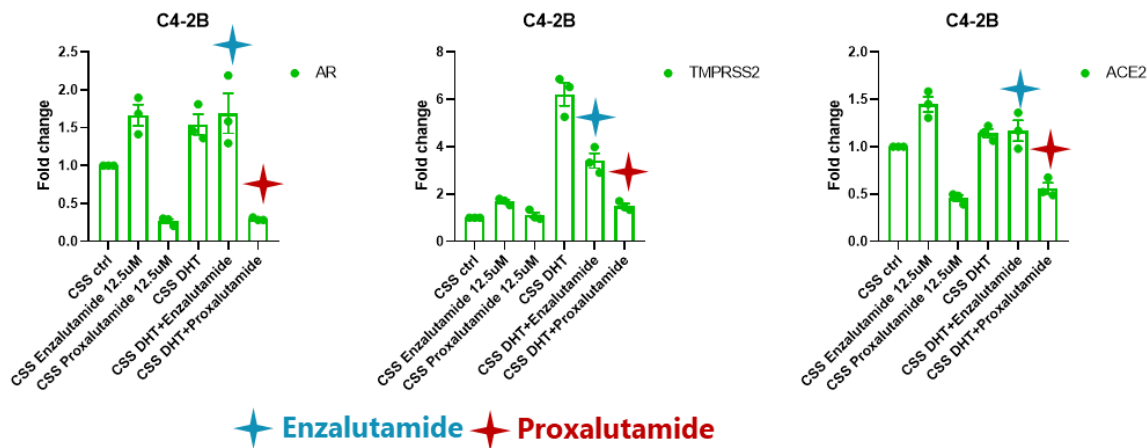


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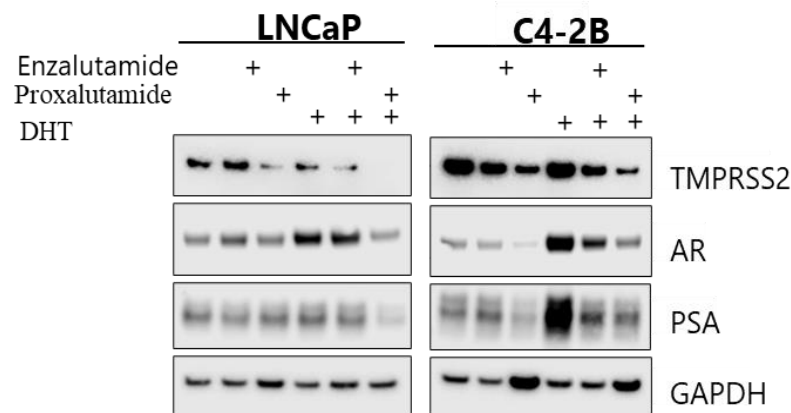
# MoA of Proxalutamide (1) : More Effectively Downregulates ACE2 and TMPRSS2 Expression than Enzalutamide

Proxalutamide more effectively downregulates TMPRSS2 and ACE2 genes and proteins expression than enzalutamide, and is effective in both androgen dependent and independent LNCaP cell lines

## mRNA Expression of AR, TMPRSS2, ACE2



## AR and TMPRSS2 Protein Expression



Note: C4-2B is an androgen-independent variant of the LNCaP cell line; LNCaP is an androgen-dependent cell line; CSS = Charcoal Stripped Serum; DHT = Dihydrotestosterone



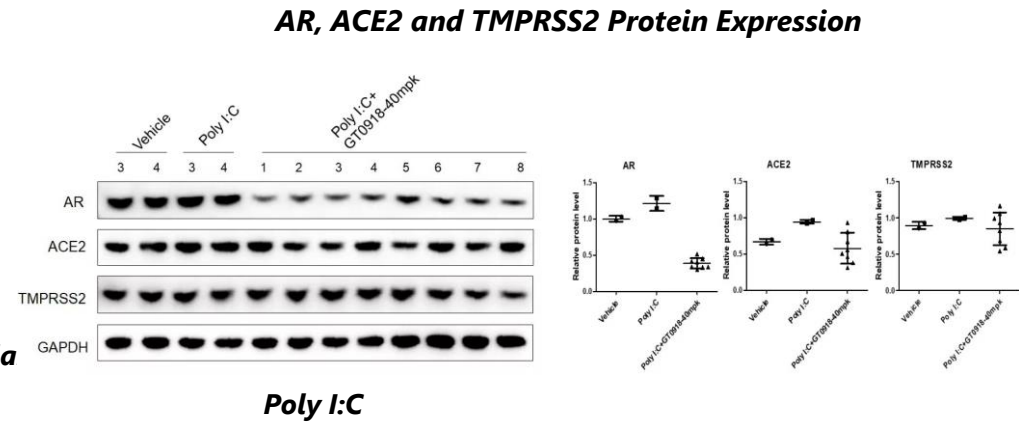
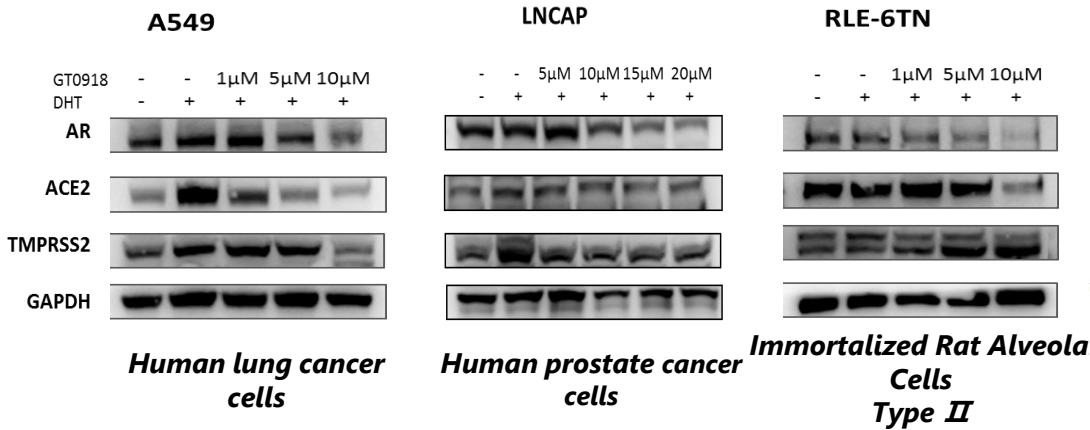
Source: Michigan Center for Translational Pathology, University of Michigan

2

# MoA of Proxalutamide (1) : Down Regulation of ACE2 and TMPRSS2 Expression in vitro and in vivo

## Proxalutamide Down-regulated ACE2 and TMPRSS2 Protein Expression

## Proxalutamide Down-regulated ACE2 and TMPRSS2 Expression in vivo



Proxalutamide inhibited ACE2 and TMPRSS2 protein expression in human lung and prostate cancer derived cells and normal lung epithelial cells, suggesting proxalutamide can **block SARS-CoV-2 cellular entry into host cells**.

ACE2 and TMPRSS2 were down-regulated in Balb/c mice with treatment with Proxalutamide, confirming AR-signaling regulates ACE2 and TMPRSS2 in vivo.

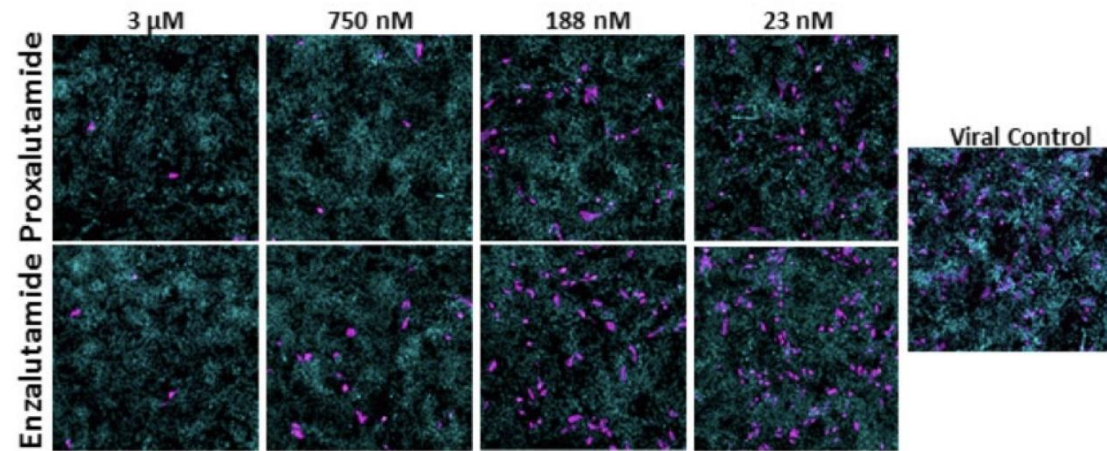
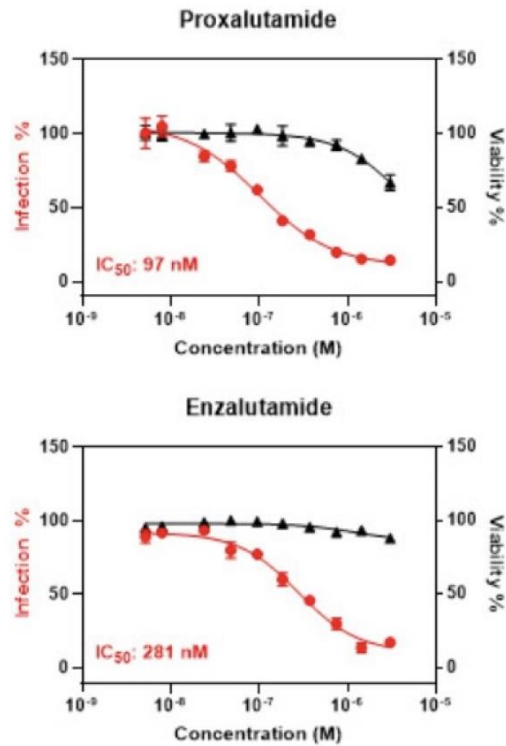


Sources: 1. Wu, Siqi et al, SSRN Electronic Journal. doi:10.2139/ssrn.3580526. ISSN 1556-5068



# MoA of Proxalutamide (1) : With Lower Concentration in Inhibiting SARS-CoV-2 Infection

2



The  $IC_{50}$  is the concentration of drug required for 50% inhibition.

## In-vitro result

**Proxalutamide  $IC_{50}$  = 97 nM**  
**vs.**  
**Enzalutamide  $IC_{50}$  = 281 nM**

## Conclusion

*Proxalutamide is 3-fold more potent than enzalutamide in inhibiting SARS-CoV-2 infection in LNCaP Cells.*

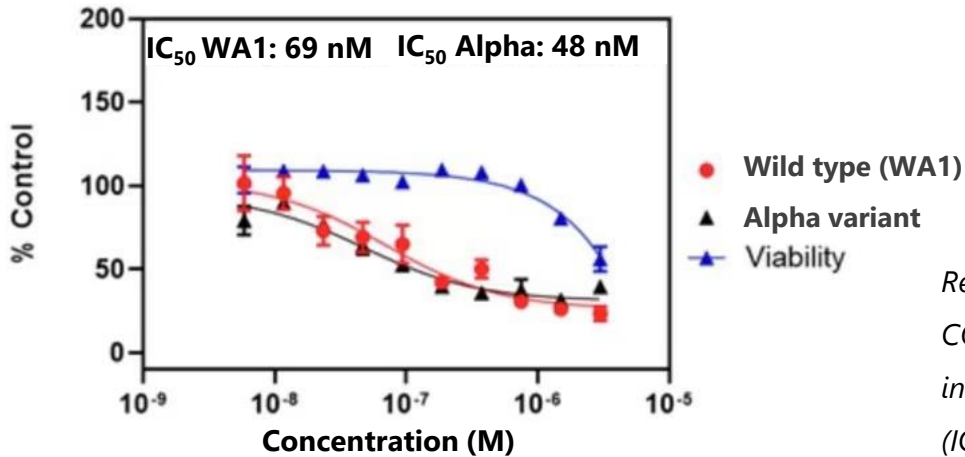
Source: Michigan Center for Translational Pathology, University of Michigan



# MoA of Proxalutamide (1) : Inhibits SARS-CoV-2 Alpha and Delta Variants

2

## Proxalutamide inhibits SARS-CoV-2 alpha variant



### SARS-COV-2 WA1

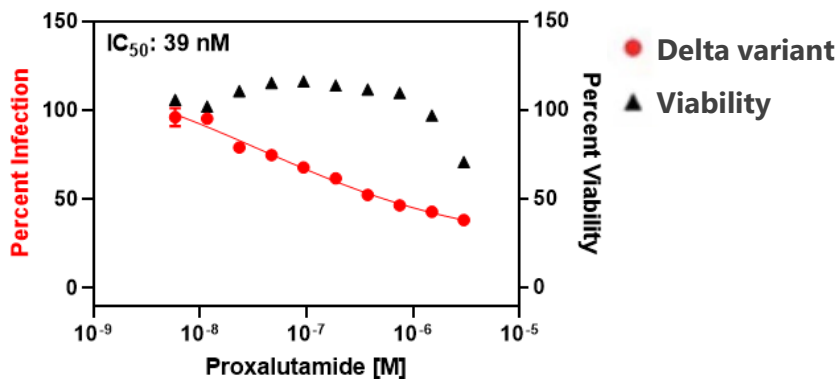
**Proxalutamide IC<sub>50</sub> = 69 nM**

### SARS-CoV-2 alpha variant

**Proxalutamide IC<sub>50</sub> = 48 nM**

Result: Proxalutamide effectively inhibited SARS-COV-2 WA/01-2020 and SARS-COV-2 B.1.1.7 variant(alpha variant) strains infection in AR positive LNCaP cells in a dose-dependent manner, with concentration that inhibits response by 50% (IC<sub>50</sub>) values of 69 and 48 nM, respectively

## Proxalutamide inhibits SARS-CoV-2 delta variant



### SARS-CoV-2 delta variant

**Proxalutamide IC<sub>50</sub> = 39 nM**

Result: Proxalutamide effectively inhibited delta variant strains infection in AR positive LNCaP cells, with concentration that inhibits response by 50% (IC<sub>50</sub>) values of 39 nM



Source: Michigan Center for Translational Pathology, University of Michigan

## 2 MoA of Proxalutamide (1) : Inhibits SARS-CoV-2 Variant

- So far, the *in vitro* studies in the P3 laboratory have demonstrated that proxalutamide can effectively inhibit infections caused by the Alpha and Delta variants.
- The outcome of genome sequencing on COVID-19 inpatients in Brazil has shown that proxalutamide has effectively treated inpatients infected by Gamma variant.
- The SARS-CoV-2 Gamma (P.1) variant came to dominated in Brazil since 12/2020 and has spread to many countries out of Brazil.

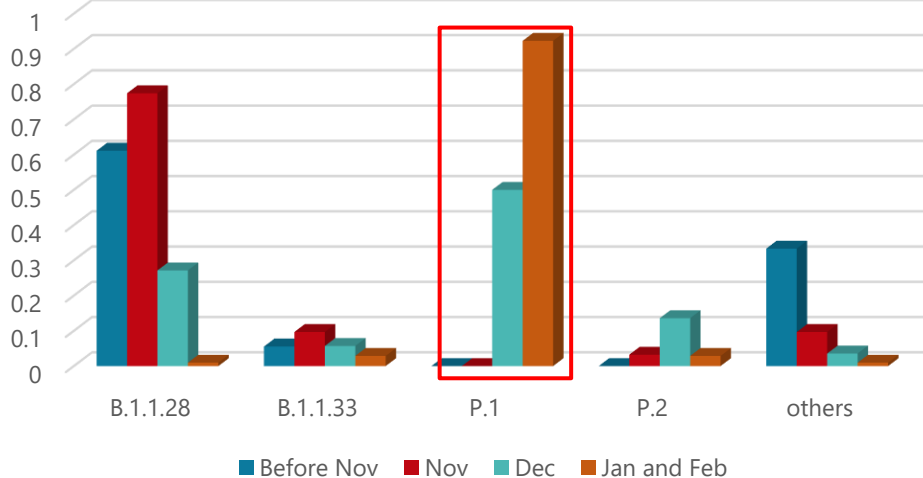
**SARS-CoV-2 Variants in Brazil (No. (%))**

Time Period	P.1	P.2	B.1.1.28	B.1.1.33
2021 Jan & Feb	<b>96 (92%)</b>	3 (3%)	1 (1%)	3 (3%)
2020 Dec	<b>70 (50%)</b>	19 (14%)	38 (27%)	8(6%)
2020 Nov	<b>0</b>	1 (3%)	24 (77%)	3(10%)
Before 2020 Nov	<b>0</b>	0	11 (61%)	1(6%)

**SARS-CoV-2 Variants in Amazonas (No. (%))**

Time Period	P.1	P.2	B.1.1.28	others
2021 Jan	<b>32 (91%)</b>	2 (6%)	0	1 (3%)
2020 Dec	<b>28 (51%)</b>	6 (11%)	17 (31%)	4 (7%)
2020 Nov	<b>0</b>	1 (4%)	19 (79%)	4 (17%)

**SARS-CoV-2 Variants in Brazil (2020 - 2021)**



Data resource: GISAID N = 293

**Figure 1. Municipalities of the Amazonas state with SARS-Cov-2 P.1 lineage samples sequenced in this study.**



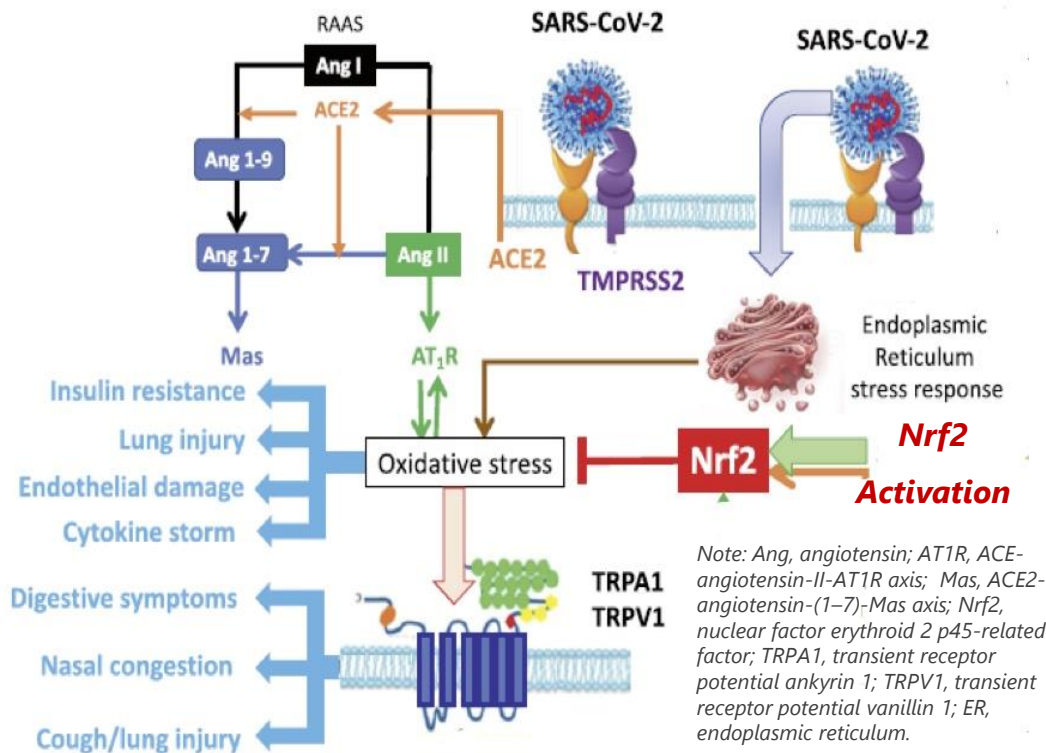
Update of the SARS-CoV-2 genomic surveillance in the amazonas state, Brazil, [https:// virological.org](https://virological.org).



# MoA of Proxalutamide (2) : Upregulation of Nrf2 Signaling Inhibits the Overproduction of Proinflammatory Cytokines

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## Nrf2 Can Downregulate the Oxidative Stress from the AT1R Axis as Well as in the ER



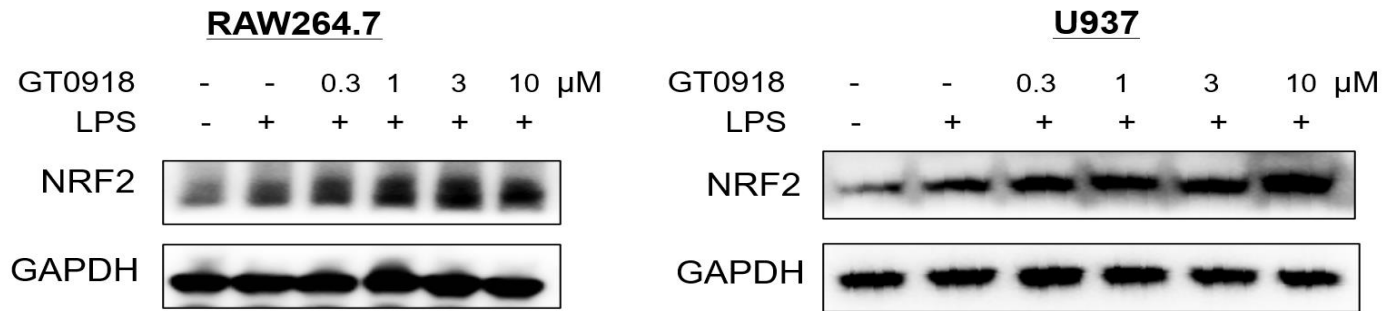
- A common denominator in all conditions associated with COVID-19 appears to be the impaired redox homeostasis, responsible for the accumulation of reactive oxygen species (ROS).
- SARS-CoV-2 binds to ACE2, and ACE2 downregulation enhances the AT1R axis leading to oxidative stress generation.
- In particular, the upregulation of Nrf2 signaling inhibits the overproduction of **IL-6, proinflammatory cytokines (TNF- $\alpha$ ), and chemokines.**
- It also limits the activation of nuclear factor-kappa b (NF $\kappa$ B) which is also involved in oxidative stress.



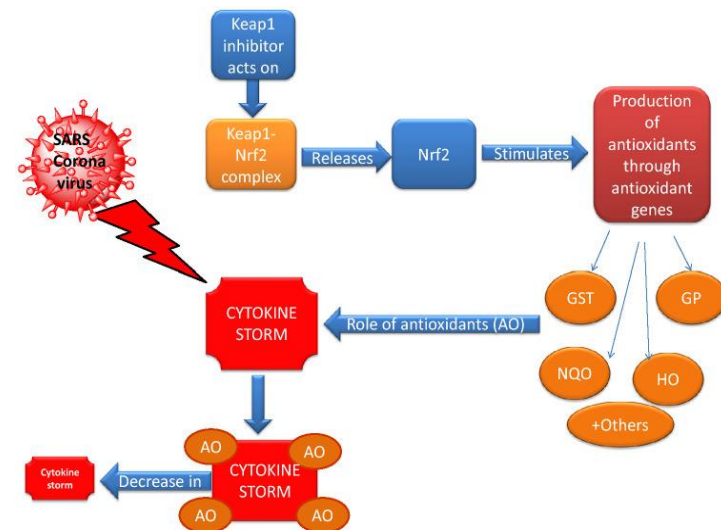
# MoA of Proxalutamide (2) : Increased the Protein Expression of Nrf2 in vitro

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**Proxalutamide upregulated Nrf2 protein expression in RAW264.7 and U937 cells**



**Nrf2 Activation Helps to Counteract Symptoms Induced by the Cytokine Storm in COVID-19**



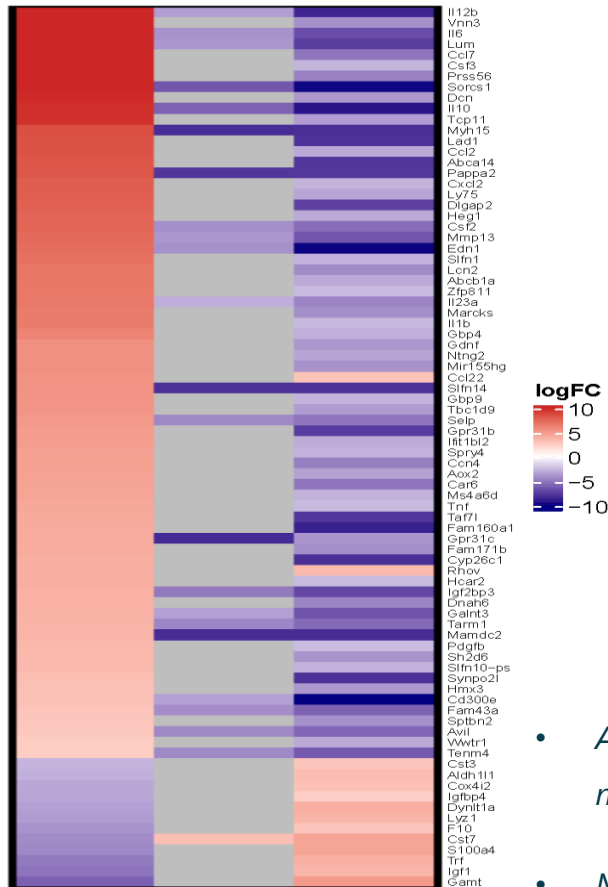
Source: Singh E, et al. Management of COVID-19-induced cytokine storm by Keap1-Nrf2 system: a review. *Inflammopharmacology*. 2021. <https://doi.org/10.1007/s10787-021-00860-5>; Prof. Qin Jun from Beijing Proteome Research Center

# MoA of Proxalutamide (2) : Regulated Inflammation Related Pathway in RAW264.7 Cells

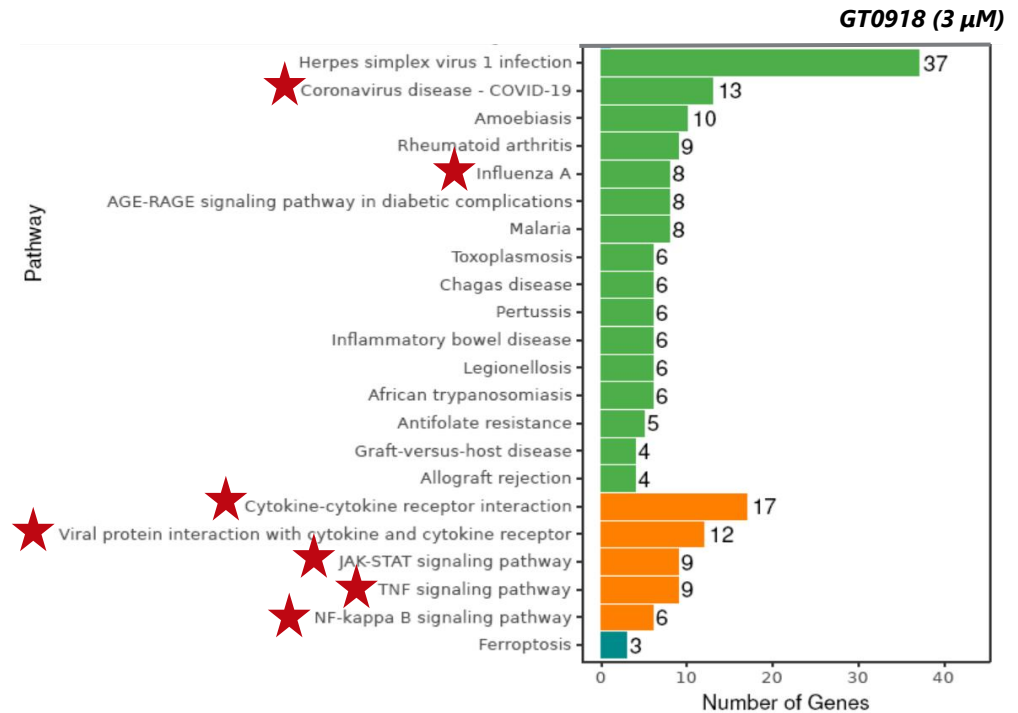
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## LPS-induced RAW264.7 Cell

Vehicle GT0918-1 $\mu$ M GT0918-3 $\mu$ M



## Functional Enrichment of Differentially Expressed Genes

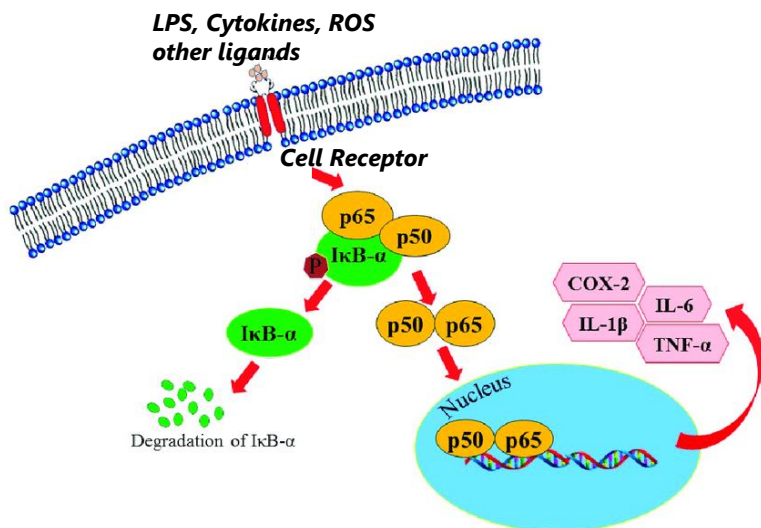


- Among the differentially expressed genes, **68** genes were down-regulated in a dose-dependent manner and **12** genes were up-regulated with the treatment of Proxalutamide.
- Most of these genes were enriched in **antiviral** and **immune regulation-related** pathways.

# MoA of Proxalutamide (2) : Down-Regulated I $\kappa$ B $\alpha$ Phosphorylation and Attenuated NF- $\kappa$ B Signaling

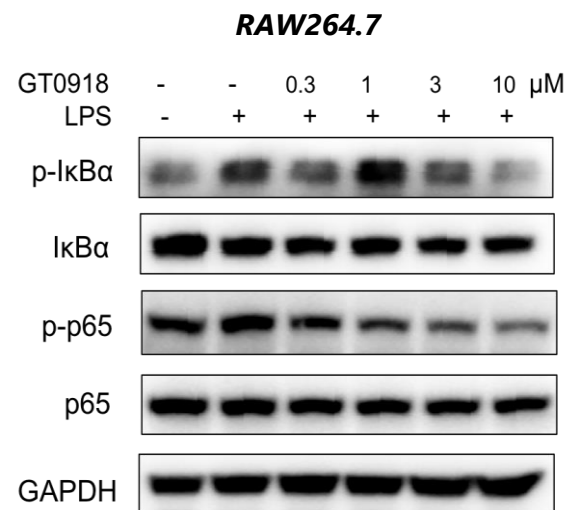
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## NF- $\kappa$ B Signaling Pathway Regulates the Expression of Various Pro-inflammatory Genes



- **NF- $\kappa$ B is a heterodimer consisting of p65 and a p52 or p50. Inactivated NF- $\kappa$ B binds with I $\kappa$ B- $\alpha$ .**
- **Phosphorylation of I $\kappa$ B- $\alpha$  results in the dissociation of NF- $\kappa$ B from I $\kappa$ B- $\alpha$ , allowing the translocation of heterodimer into the nucleus and binding to the promoters of pro-inflammatory genes, such as IL-1 $\beta$ , IL-6, TNF- $\alpha$ , and cyclooxygenase (COX)-2.**

## Proxalutamide Down-Regulated the Phosphorylation of I $\kappa$ B $\alpha$ & p65 in NF $\kappa$ B Pathway



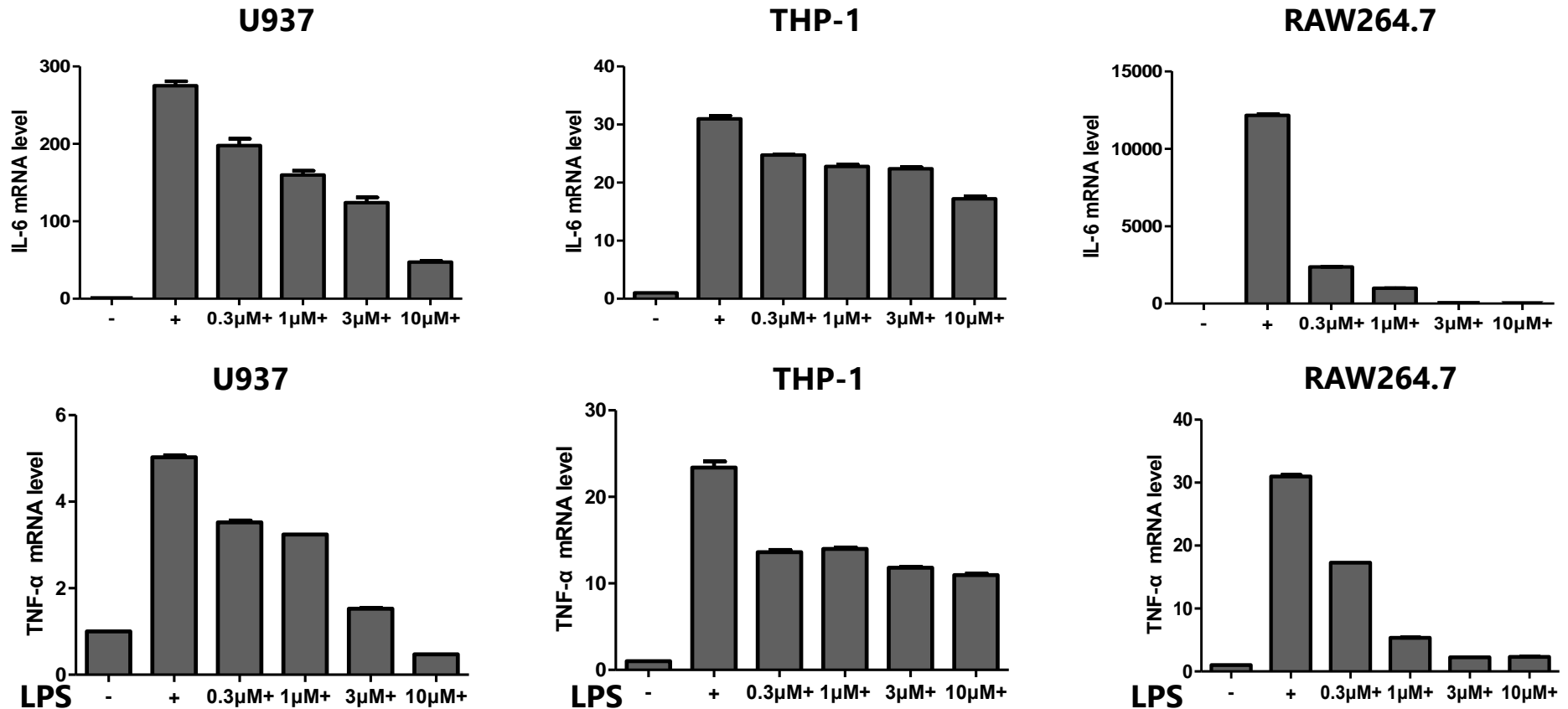
- *Proxalutamide down-regulated the activation of p65 by decreasing phosphorylation of I $\kappa$ B $\alpha$ , and inhibited the activation of NF $\kappa$ B pathway in a dose-dependent manner, suggesting the possible mechanism of Proxalutamide on immune regulation.*



Source: Molecules, 2018, 23, 597; doi:10.3390/molecules23030597.

# MoA of Proxalutamide (2) : Dose-Dependently Inhibited LPS-induced TNF- $\alpha$ and IL-6 Expression at mRNA Level in vitro

2



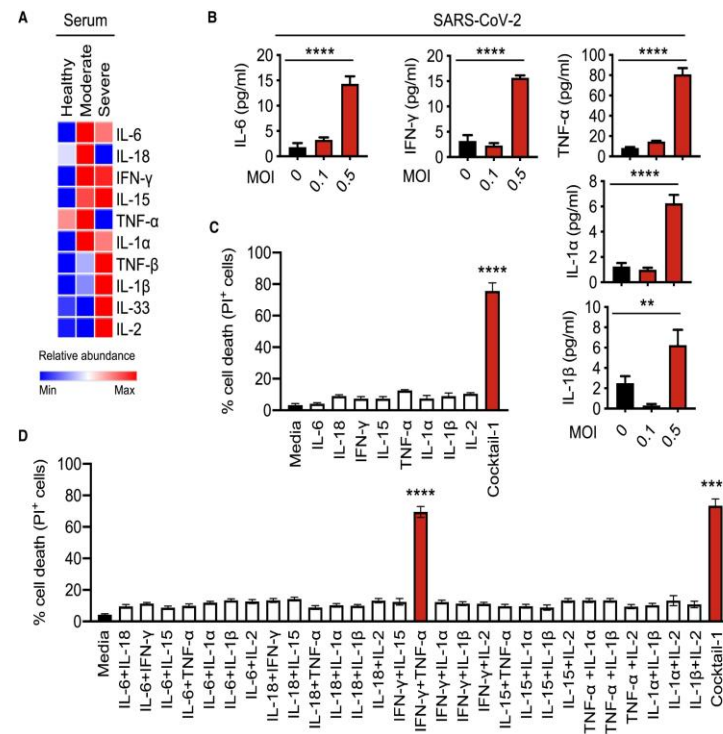
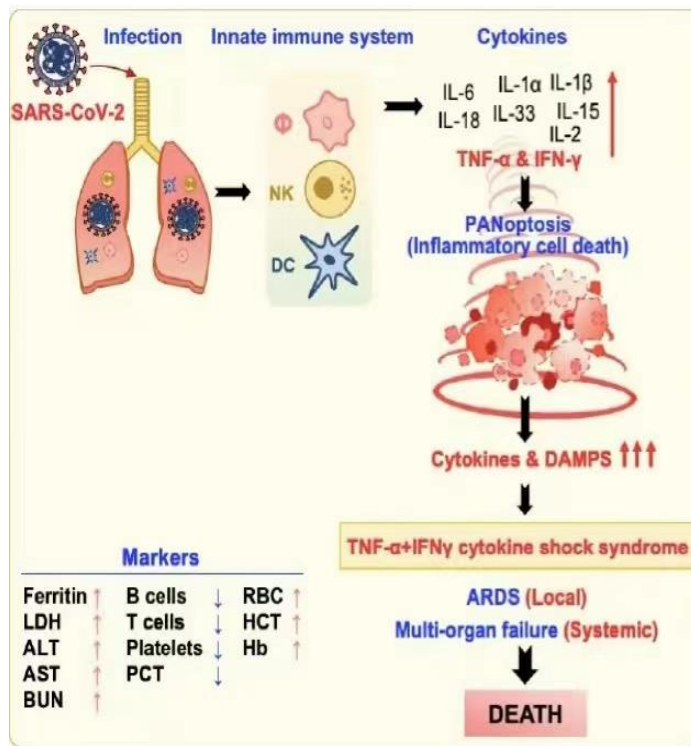
- Proxalutamide inhibited LPS-induced TNF- $\alpha$  and IL-6 expressions in RAW264.7, THP-1 as well as AR-negative U937 cells, in a dose dependent manner. (18 hours incubation)



# MoA of Proxalutamide (2) : Down-Regulated the Expression of STATE1 and STATE3 on Downstream of TNF- $\alpha$ and INF- $\gamma$ -Induced Inflammatory Cell Death Pathway

2

## TNF- $\alpha$ and IFN- $\gamma$ Synergize to Drive the Cytokine Storm and Cell Death Associated with COVID-19



While multiple inflammatory cytokines are produced by innate immune cells during SARS-CoV-2 infection, only the combination of TNF- $\alpha$  and IFN- $\gamma$  induced inflammatory cell death characterized by inflammatory cell death, PANoptosis.

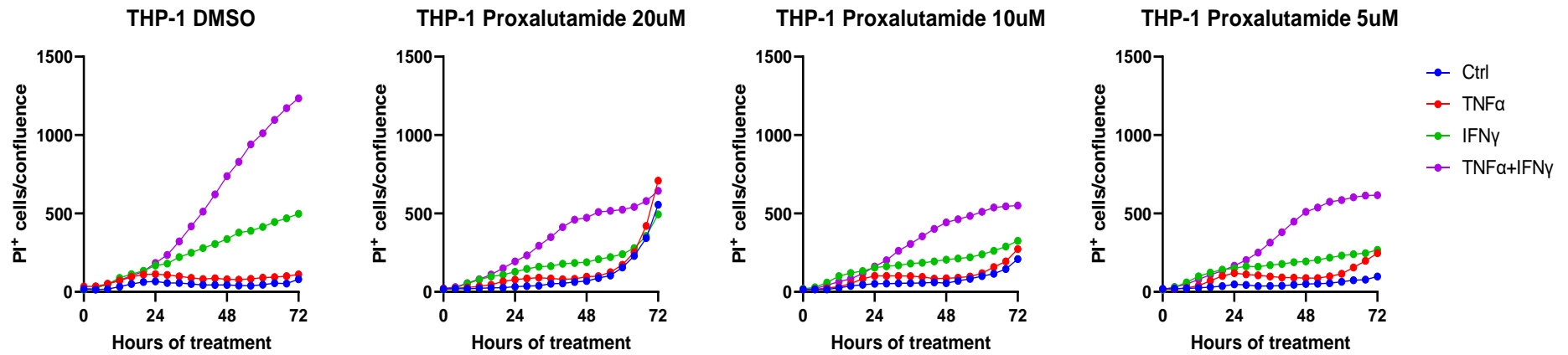
**Source:** Karki et al. Synergism of TNF- $\alpha$  and IFN- $\gamma$  Triggers Inflammatory Cell Death, Tissue Damage, and Mortality in SARS-CoV-2 Infection and Cytokine Shock Syndromes. *Cell*, 2021 (184), 149–168.



2

# MoA of Proxalutamide (2) : Inhibited TNF- $\alpha$ and IFN- $\gamma$ -induced Inflammatory THP-1 Cell Death

- THP-1 human macrophages were stimulated with TNF- $\alpha$  and IFN- $\gamma$  to induce inflammatory cell death and then were treated with proxalutamide (5  $\mu$ M, 10  $\mu$ M and 20  $\mu$ M) for 72 hr.



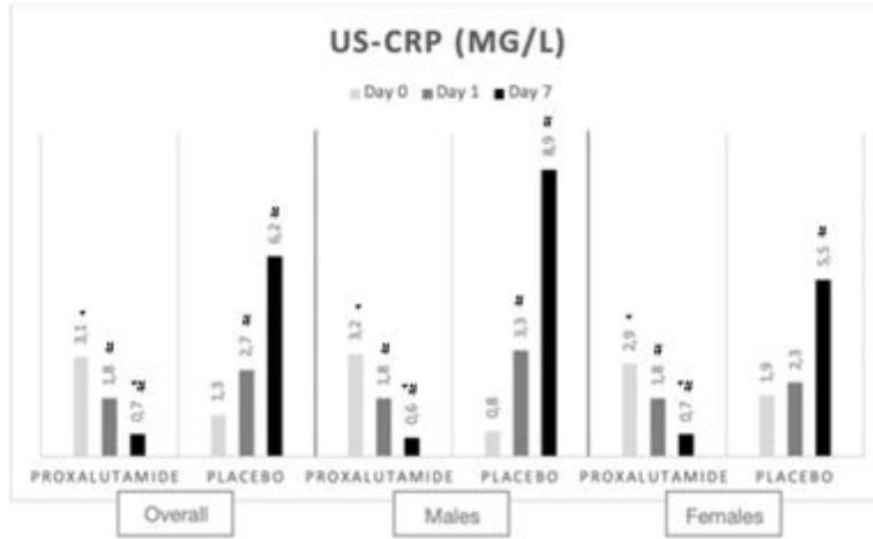
- Proxalutamide protected TNF- $\alpha$  + IFN- $\gamma$  induced cell death in dose dependent manner.**



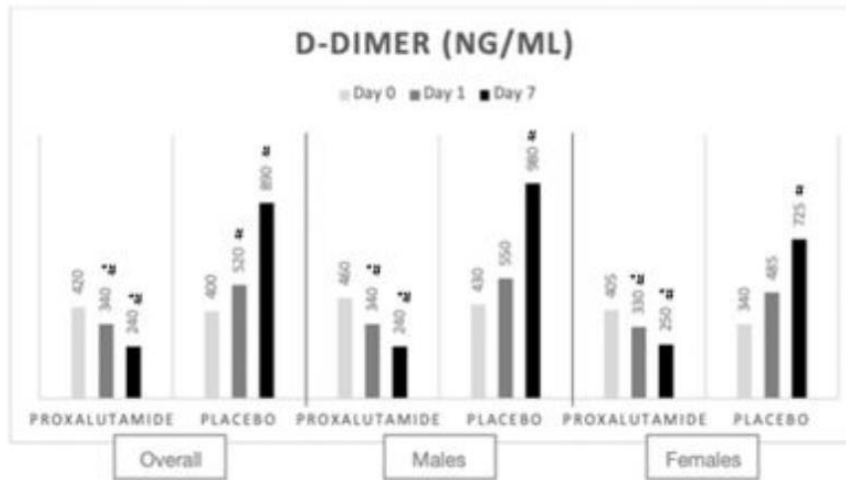
Source: Michigan Center for Translational Pathology, University of Michigan

# MoA of Proxalutamide (2) : Significantly Reduces Inflammatory and Thrombotic Markers

2



1. Ultrasensitive C-reactive protein is a protein the liver produces in the presence of infection or inflammatory disease



2. D-dimer levels are used as a predictive biomarker for the blood disorder, disseminated intravascular coagulation and in the coagulation disorders associated with COVID-19 infection

\* = p < 0.05 versus placebo; # = p < 0.05 versus day 0

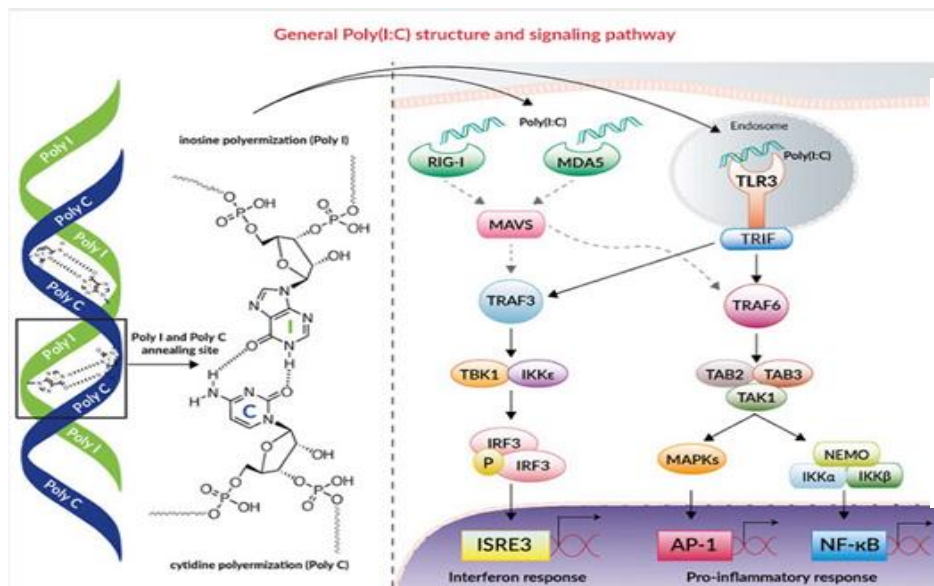
Source: 1. Flavio A. Cadegiani et al, doi: <https://doi.org/10.1101/2021.07.24.21261047>; 2. "Assessing Cardiovascular Risk with C-Reactive Protein". [www.hopkinsmedicine.org](http://www.hopkinsmedicine.org). 3. "D-dimer", Wikipedia



# MoA of Proxalutamide (2) : Inhibited Acute Immune Response in Poly I:C-induced Acute Lung Injury Animal Model

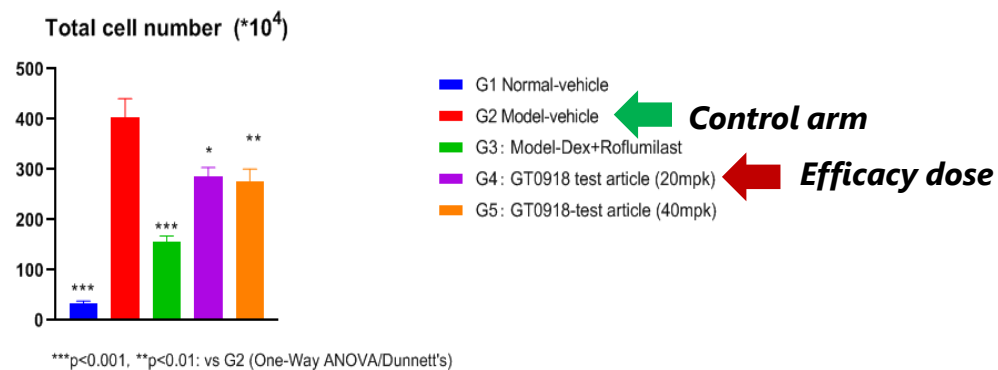
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## General Poly I:C Structure and Signaling Pathway



- Polyinosinic: polycytidylic acid (usually abbreviated as poly I:C) is a double-stranded RNA which stimulate the Toll-like receptor 3 (TLR3).
- Poly I:C induced acute lung injury model is a common model for scientific research on the immune system
- This model may simulate Covid-19 patient pathophysiological processes, like the secretion of IL-6 and TNF-α increased in bronchoalveolar lavage fluid (BALF)

## Effect of Proxalutamide in Poly I:C-induced Viral Infection Mouse Model



**Note:** Dex = Dexamethasone; Roflumilast = PDE4 inhibitor. These two drugs are only for the model validation

- GT0918 at 20 mpk/BID (human equivalent dose= 100mg/BID) level is an efficacy dose to reduced infiltrated white blood cell counts in lungs in Poly I:C induced viral infection mouse model



Source: Gu, Tingxuan, etc. "Molecular mechanism of SARS-CoV-2 components caused ARDS in murine model": 2020.06.07.119032. doi:10.1101/2020.06.07.119032v4.



## 2 HED Safety Profile from SD Rats Model

Repeat-Dose Toxicity in SD Rats	Dose (mg/kg)	NOAEL (no observed adverse effect level)	HED (Human equivalent dose)
4-week	20,60,120	60mg/kg	60mg/kg ÷ (36.88/6.6) ×60kg= <b>644mg</b>
13-weeks	20,45,90	90mg/kg	90mg/kg ÷ (36.88/6.6) ×60kg= <b>966mg</b>
26-weeks	20,45,90	45mg/kg	45mg/kg ÷ (36.88/6.6) ×60kg= <b>483mg</b>

$HED = NOAEL(mg/kg) \div [km_{human}/km_{animal}] * Human\ Weight$

$km_{human} = 36.88, km_{animal} = 6.6, Human\ Weight = 60kg$

Note:  $Km = Dose(mg/m^2) \div Dose(mg/kg)$  ←

$$= [10 \times Dose(mg/kg) \times W + (10^{(0.698 \times \log_{10} \frac{W}{10} + 0.8762)})] \div Dose(mg/kg)$$
 ←

$$= (10 \times W) \div 10^{(0.698 \times \log_{10} \frac{W}{10} + 0.8762)}$$
 ←

The weight in three repeat dose toxicity studies in rats was about 250g.

The human equivalent NOAELs for a 60kg man are 644mg for 4 weeks, 966mg for 13 weeks, and 483mg for 26 weeks, separately observed in the rat model, which means **200mg/300mg for 2 weeks has a good safety profile in COVID-19 clinical trials.**

# Sufficient Clinical Exposure of Proxalutamide to Be Effective In-

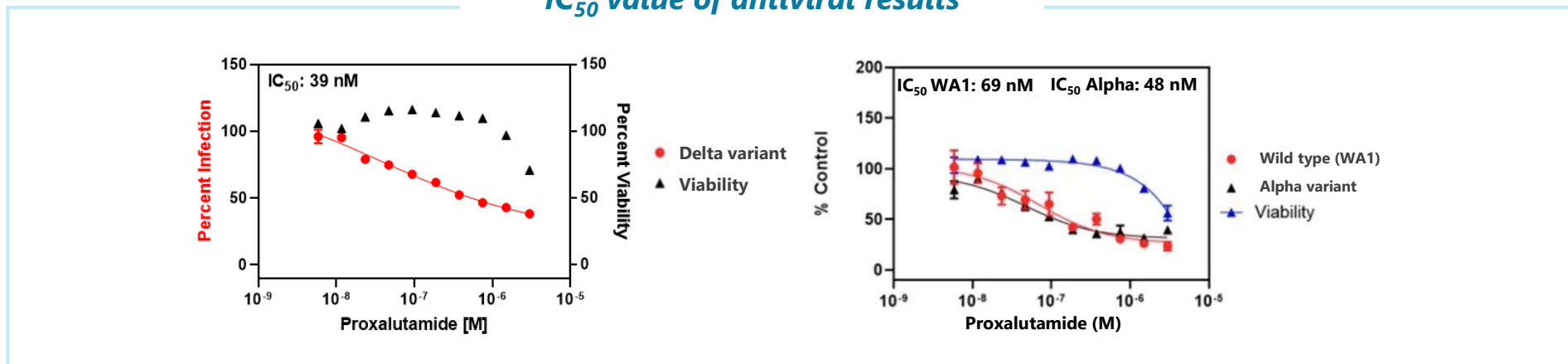
## 2 Vivo

	A	B	C	
Single dose of 200mg	C <sub>max</sub> (ng/mL)	C <sub>max</sub> (μM)	Free Drug (nM)	
Pre-meal	6580	12.7	152.6	686.6
Post-meal	12200	23.6	282.9	1273.0

**Note:** PPB(Plasma protein binding): 94.6%~98.8%; MW(molecular weight):517.5

$$A/MW=B, B*(1-PPB)=C$$

### IC<sub>50</sub> value of antiviral results



Following a single oral dose of 200mg, GT0918 geometric mean C<sub>max</sub> was 12.7 μM and 23.6 μM following pre-meal and post-meal conditions respectively. Given the consideration of human PPB is 94.6%~98.8%, the free drug is 152.6~686.6 nM and 282.9~1273.0 nM, which is **far higher than IC<sub>50</sub> value of antiviral results**(69 nM for wild type/ 39nM for delta variant/ 48nM for alpha variant), **thus sufficient to be effective in vivo.**



# 3 Proxalutamide (GT0918): Ongoing mCRPC Clinical Trials

## Phase III Clinical Trials in China (Monotherapy)

Conducting data analysis

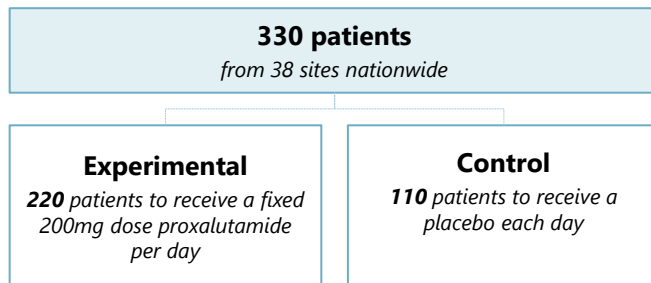
CTR20180849

### Design

To evaluate the impact on the rPFS and overall survival time, the safety, as well as the relationship between the discovery of biomarkers and the efficacy of proxalutamide in mCRPC patients who have failed Abiraterone and Docetaxel treatments

### Patient Enrolment

Multi-centre, randomised, double blind clinical trials



Each treatment cycle lasts 28 days

### Co-primary endpoints

Radiographic progression-free survival (rPFS), overall survival(OS)

## Phase III Clinical Trials in China (Combo-therapy with Abi)

Enrolled total 718 patients on Feb 24, 2022

CTR20182095

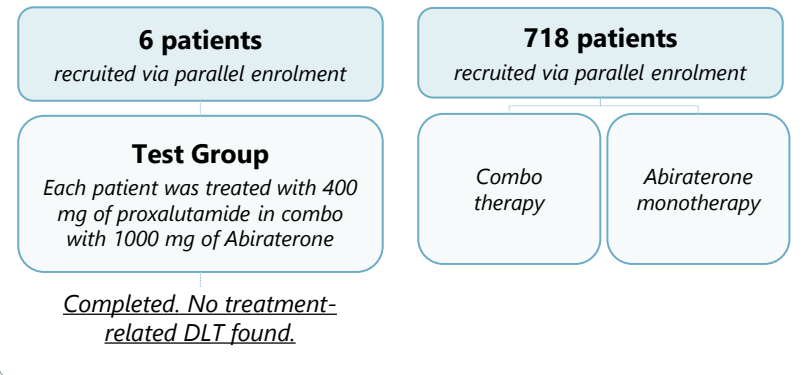
### Design

To evaluate the efficacy and safety of proxalutamide's combination therapy with Abiraterone in comparison with Abiraterone in monotherapy as a **first-line treatment for mCRPC**

### Patient Enrolment

**1<sup>st</sup> Phase:** Multi-centre, open, one-arm design to assess safety and tolerability

**2<sup>nd</sup> Phase:** Evaluation of rPFS, pharmacodynamic indicators, safety and others



### Primary endpoints

Radiographic progression-free survival (rPFS)

# 3 Proxalutamide (GT0918): Ongoing mCRPC Clinical Trials

## Phase II Clinical Trials in US (Monotherapy) NCT03899467

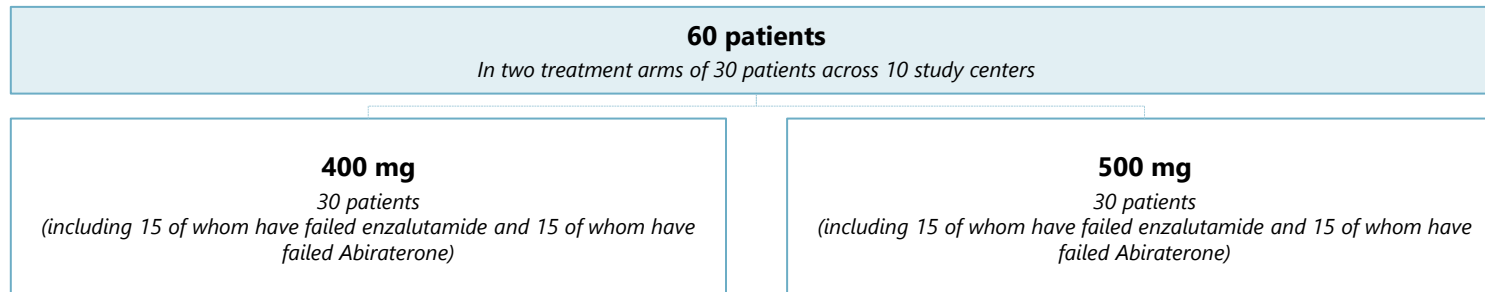
Will conduct data analysis in Q2 2022

### Design

To evaluate the safety and tolerability of proxalutamide in patients with mCRPC who have **failed Abiraterone or Enzalutamide treatment**

### Patient Enrolment

Multi-centre, open-label, randomised study



### Endpoints

Primary endpoints: 1) recommended Phase 2 dose; 2) Number of Patients With Toxicity of proxalutamide

Secondary endpoints: 1) >50% PSA suppression; 2) percentage of radiographic disease progression; 3) radiographic and bone progression time; 4) the time to PSA progression; 5) exploratory biomarkers: cell free circulating tumor DNA (ct-DNA)/RNA (ct-RNA); 6) exploratory biomarkers: Circulating tumor cells (CTC)



# Proxalutamide: Metastatic Breast Cancer



## Phase Ic Clinical Trials in China (CTR20191063)

To evaluate the safety, pharmacokinetic characteristics and initial efficacy of Proxalutamide in combination with Exemestane, Letrozole and Fulvestrant in patients with HR+ and AR+ metastatic breast cancer

**Stage 1: Introduction Period** to collect pharmacokinetics data of individual drugs

**Letrozole**  
14 days (6 patients)

**Exemestane**  
14 days (6 patients)

**Fulvestrant**  
28 days (6 patients)

**Stage 2: Combination Therapy Period** wherein Proxalutamide and the combo therapy drug will be administered with two 4 week (28 days) treatment cycles

**1<sup>st</sup> Cycle**  
Subjects will receive a DLT assessment during the 1<sup>st</sup> cycle of combination therapy

**2<sup>nd</sup> Cycle**  
Subjects will undergo a tumour imaging evaluation at the end of the 2<sup>nd</sup> cycle of treatment

**Stage 3: Extended Treatment Period** after the completion of 2 treatment cycles



**Extended Treatment**  
If a subject's disease is clinically relieved or stable and well tolerated and if the subject is willing to continue taking the test drug, the investigator may continue to give the patient extended treatment until there is disease progression

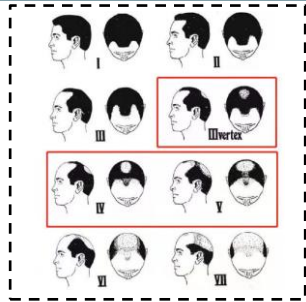


Source: Prospectus

# Pyrilutamide: Utilizing our Proprietary AR Capabilities to Address Androgenic Alopecia

4

## Androgenic alopecia – A growing concern globally



- Common form of scalp hair loss affecting **both men and women**
  - Rapidly growing** concerns among all age group due to lifestyles and stress
- Stage III vertex-V in Norwood-Hamilton scale

## Underpenetrated market lack of novel treatment

Androgenic alopecia is a common form of scalp hair loss that affects both men and women

<p><b>Finasteride</b>   Oral: Approved for androgenic alopecia by the US FDA in 1997                  Spray: Approved in Luxembourg and Italy in 2020; approved in Portugal and Germany in 2021</p>	<p><b>Minoxidil</b>   Approved for androgenic alopecia in 1988 and as an OTC drug in 1996 by the US FDA</p>
--	--

Only two products\* available in the market for androgenic alopecia,

and no novel treatment approved in the last 22 years  
 \* Dutasteride was approved for the treatment of AGA by South Korea and Japan in 2009 and 2015 separately, but was approved by FDA only for the treatment of benign prostatic hyperplasia (BPH) in 2001

### Significant limitations and side effects in current treatments

Finasteride	Minoxidil
<ul style="list-style-type: none"> <li>Severe <b>sexual adverse effects</b></li> <li><b>Orally</b> taken drug</li> <li>Only approved and found effective for use in men</li> </ul>	<ul style="list-style-type: none"> <li>Fragmented market after patent expiry in 1998</li> <li><b>No clear MoA</b></li> </ul>

- Strong demand** by people with AGA for the medical treatment with **proven efficacy and safety**
- Treatment rate** for hair loss remains **high** and is expected to **improve** consistently each year
- OTC options and hair transplant are **rapidly growing** due to the **lack of effective and safe** medical options

### Prevalence<sup>1</sup>

### Market potential<sup>2</sup>



134 million



Market Size of Drugs Approved for Androgenic Alopecia  
**CNY5.04bn** in 2028



83 million



Market Size of Drugs Approved for Androgenic Alopecia  
**US\$1.4bn** in 2028

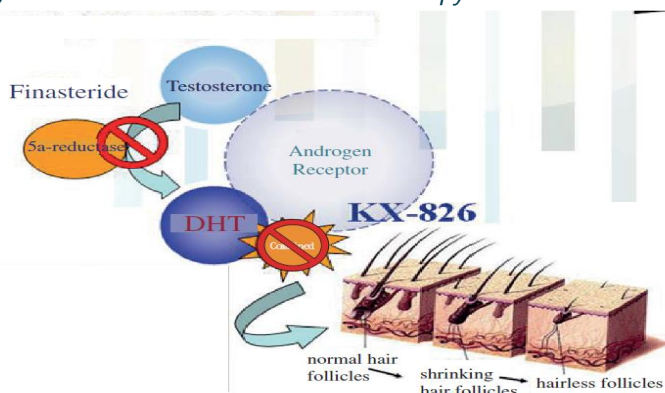
Source: Company Prospectus, Frost & Sullivan analysis,  
 Note: 1. Data in 2019 2. Refer to drugs (excluding consumer goods) 3. USD/CNY = 6.67



# 4 Ppyrilutamide: Androgenetic Alopecia

## Mechanism of Action

The combination process of **DHT and receptors affects the hair follicle cells**, which leads to obstruction of hair follicles and results in the shrinkage of hair follicles due to their ability absorb nutrients. It leads to excessive hair loss, and eventually to baldness without immediate therapy.



KX-826 is being developed for topical application to locally block the androgen mediated signalling **by competing androgen to bind to AR** in the targeted tissues instead of reducing androgen levels systemically

## Results from Previous Clinical Trials

### Phase I/Ib clinical trials in China and US

- ✓ **Safety:** There were **no ≥ grade 3 SAE**. All AEs related to the drug were "contact dermatitis" **and all were mild**, which recover/heal in a short time. The contact dermatitis may be caused by excipients.
- ✓ **PK:** The **blood concentration is extremely low**.

## Clinical Trials

### Ongoing

- ✿ **Phase III Clinical Trials For AGA Male Adults In China** (randomized, double-blind, placebo-controlled, multi-regional)
  - Sample size = 416
  - Primary endpoint: the change from baseline in non-vellus target area hair counts (TAHC) at week 24
  - Commenced first patient enrollment on Dec 31, 2021
- ✿ **Phase II Clinical Trials For AGA Female Adults In China** (randomized, double-blind, placebo-controlled, multi-regional)
  - Sample size = 160
  - Primary endpoint: the change from baseline in non-vellus target area hair counts (TAHC) at week 24
- ✿ **Phase II Clinical Trials For AGA Male Adults In US** (randomized, double-blind, placebo-controlled)
  - Sample size = 120
  - Primary endpoint: the change from baseline in non-vellus target area hair counts (TAHC) at week 24

### Completed

- ✿ **Phase II Clinical Trials For AGA Male Adults In China**(randomized, double-blind, placebo-controlled, multi-regional)
  - Sample size = 120, randomized at the ratio 1:1:1:1 to 4 arms: (2.5mg) 0.25% Ppyrilutamide BID, (5mg) 0.5% Ppyrilutamide QD, (5mg) 0.5% Ppyrilutamide BID, and Placebo.
  - Primary endpoint: the change from baseline in non-vellus target area hair counts (TAHC) at week 24
  - Results: Announced on Sep 8, 2021 that KX-826's phase II trial for male AGA adults met primary endpoints in China. The majority of AEs were mild and no SAE occurred. 5mg (0.5%) will be used in phase III trial in China
  - Expected to release detailed data in June 2022



Source: Company Prospectus, CDE

# Pyrilutamide: Utilizing our Proprietary AR Capabilities to Address Acne Vulgaris

4

## Robust Clinical Profile Target to Redefine the Market

Acne vulgaris is a chronic inflammatory dermatosis notable for open or closed comedones and inflammatory lesions

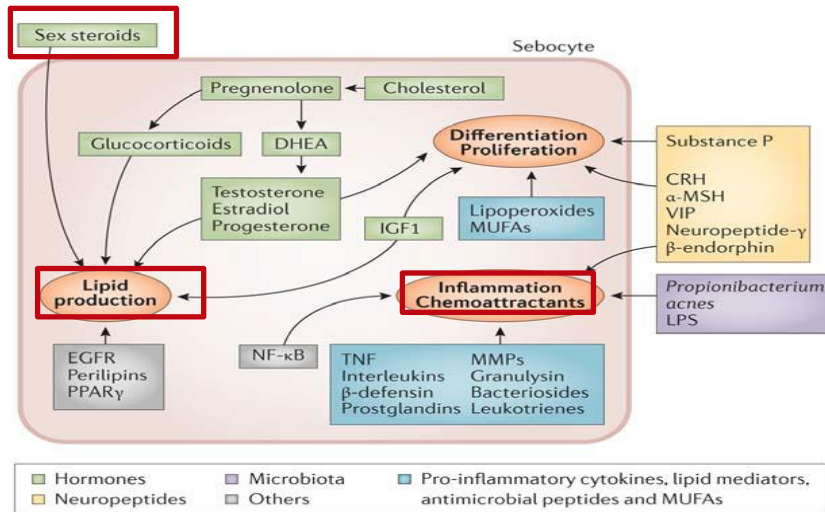
Hormonal agents, topical therapies, systemic antibiotics and isotretinoin are the prescribed treatment options



150+ million

Prevalence of acne globally aging 10 to 25 in 2018

### Pathophysiological Processes



- The pathogenesis of acne involves several processes, including sebum production and sebocyte differentiation, proliferation, and inflammation.
- These processes are regulated by circulating sex hormone levels as well as locally synthesized hormones, neuropeptides, the microbiota, and pro-inflammatory cytokines, lipid mediators, antimicrobial peptides, and monounsaturated fatty acids (MUFAs).

## Ongoing Clinical trials

- Received IND approval for acne vulgaris in China, and completed first patient enrolment of phase II trial in Jan 2022
- Expect to complete phase I/II trial and commence phase III trial in 2022

### Phase I/II clinical trials in China CTR20210427

#### Design

Evaluate the safety, tolerability, pharmacokinetics, and efficacy of pyrilutamide in subjects with mild to moderate acne vulgaris

#### Subjects Enrolment

Randomized, double-blind, placebo-controlled clinical study

224 subjects

0.25% Pyrilutamide gel QD	0.25% Pyrilutamide gel BID	0.5% Pyrilutamide gel QD	0.5% Pyrilutamide gel BID
1% Pyrilutamide gel QD	1% Pyrilutamide gel BID	Placebo QD	Placebo BID

#### Primary endpoints

Phase I: Tolerability and safety (contact dermatitis, AEs, etc.)

Phase II: Efficacy and safety (IGA Scale, facial sebum level, AEs, etc.)

\*IGA: Investigator Global Assessment

Source: Company Prospectus, Frost & Sullivan analysis, CDE





# 5 ALK-1 (GT90001): Potential First-in-class Fully Human Mab

- ◆ Conducting phase Ib/II clinical trial in combination with Nivolumab for the 2<sup>nd</sup>-line treatment of HCC in Taiwan, China
- ◆ On Feb 11, 2021, FDA greenlighted phase II clinical trial in combination with Nivolumab for the 2<sup>nd</sup>-line treatment of HCC
- ◆ On Oct 9, 2021, NMPA approved the clinical trial in combination with Nivolumab for the treatment of HCC

**Study Design in TW:** a phase I/II, open-label, single arm, dose de-escalation and expansion trial of GT90001 in combination with Nivolumab (NCT03893695)

## Study Population:

- HCC with at least one measurable lesion.
- BCLC C or B (refractory or not amenable to locoregional therapy).
- Have documented disease progression or intolerance after first-line systemic treatment with Sorafenib or Lenvatinib
- Child-Pugh score  $\leq 6$ .
- ECOG performance status: 0-1.

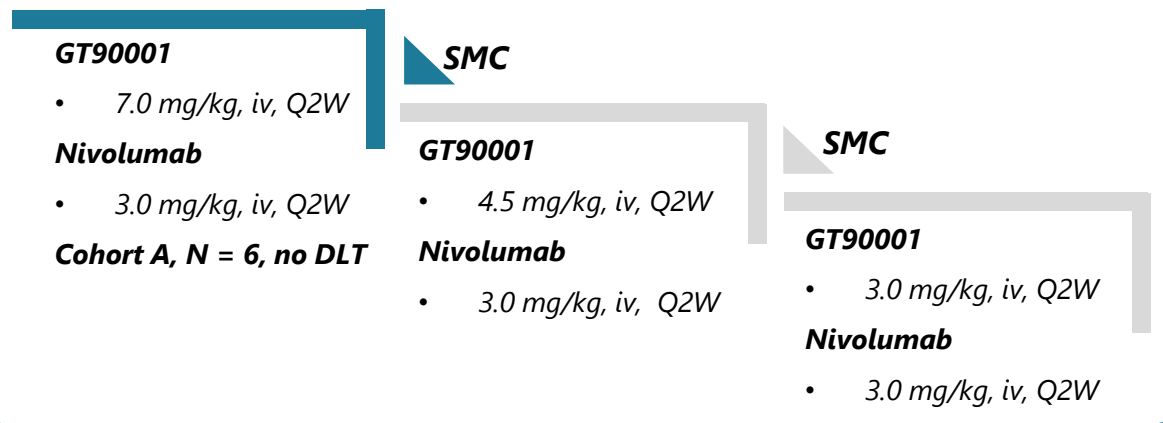
## Primary Endpoints

- Safety and tolerability

## Secondary Endpoints

- ORR (investigator)
- DOR, DCR, TTR, PFS (investigator)
- PK profile

## Stage One: Safety evaluation



## Stage Two: Dose Expansion

- **Subject Population:** same as stage one  
**N = 14** (enrollment completed in June 2020)
- **Treatment:**  
**GT90001** 7.0 mg/kg, iv, Q2W  
**Nivolumab** 3.0 mg/kg, iv, Q2W

# 5 ALK-1 (GT90001): Results of Phase II in Taiwan

## Safety Results

- No DLTs were observed in the cohort A in dose de-escalation phase.
- In total, 20/20 (100%) patients  $\geq 1$  treatment-related AE, mainly mild to moderate and easily manageable.
- Treatment related grade 3-4 AEs were reported in 6 patients (30%), including platelet count decreased (n=3, 15.0%), skin rash (n=2, 10%), Aspartate aminotransferase increased (n=1, 5%). No grade 5 AEs reported.
- 3 patients (15%) experienced treatment-related SAEs (renal dysfunction G2, hepatitis G2, hyperamylasemia G2).

## Efficacy Results

update date: 30-Sep-2020

GT90001 (7 mg/kg) + Nivolumab (3 mg/kg)	PR (N = 20)	ORR (N = 20)	ORR (confirmed) (N = 20)	SD $\geq$ 16weeks (N = 20)	DCR (N = 20)	DOR (N=8)	
						> 12months	>6months
<b>Number (%) of Patients</b>	40% (8/20)	<b>40%</b> (8/20)	25% (5/20)	10%(2/20)	50% (10/20)	12.5% (1/8)	37.5 (3/8)

- As of 30<sup>th</sup> Sep. 2020, all 20 patients had received at least one non-baseline tumor evaluation.
- Eight (8) patients achieved PR while five (5) pts achieved confirmed PR. One patient has not yet reached confirmed PR.
- Six(6)patients remain on responding status.

## PK Analysis

Tested Drug	AUC <sub>0-t</sub> (hr* $\mu$ g/mL) N=6	CL (mL/hr/kg) N=6	T <sub>1/2</sub> (day) N=6	C <sub>max</sub> ( $\mu$ g/mL) N=6
<b>GT90001</b>	20160.9 $\pm$ 37.8	0.23 $\pm$ 0.08	10.1 $\pm$ 5.1	159.3 $\pm$ 42.3
<b>Nivolumab</b>	7043.7 $\pm$ 46.1	0.179 $\pm$ 0.054	16.3 $\pm$ 4.3	50.3 $\pm$ 23.6

- In the combination, the pharmacokinetics of GT90001 and nivolumab were similar to those observed in monotherapy.
- Serum concentrations declined in a bi-exponential manner over the course of the treatment interval.
- GT90001 was slowly eliminated from the circulation.

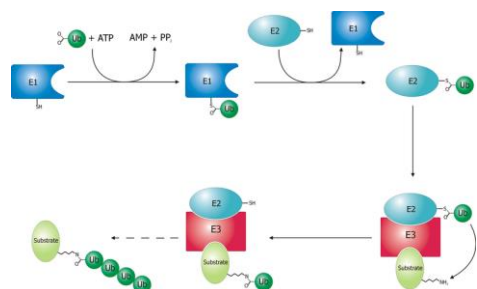


# GT20029: Potential Candidate for AGA and Acne by In-house PROTAC Platform

6

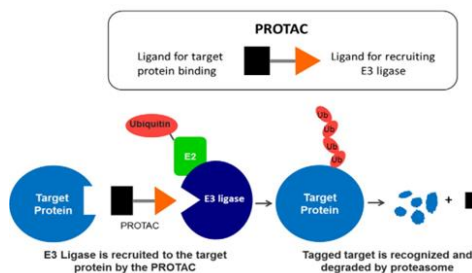
## PROTAC: PROteolysis TARgeting CHimera

**Ubiquitinproteasome system(UPS) is a natural protein degradation process**



- Much of the turnover of protein in cells is mediated by the UPS.
- Using the UPS to induce degradation of specific target proteins has been studied for decades.

## PROTAC hijacks UPS in the cell to degrade target protein



- PROTACs are heterobifunctional compounds comprising a recruiting element for a protein of interest (POI) and an E3 ligase recruiting element bound together via a linker. By bridging the gap between a POI and an E3 ligase and inducing their proximity, PROTACs can induce the ubiquitination of the POI and then degrading POI.

## MOA of GT20029

It can selectively degrade Androgen Receptor in cell based assays. It will be applied locally to affected areas for treatment.

## Advantage of GT20029

GT20029 has the totally different MOA for treating androgenetic alopecia and acne vulgaris. It has the potential to redefine the market given its treatment avoids notable side effects that have deterred users from accepting the treatment



It has all the advantages that pyrilutamide has over other treatments currently on the market.



Additionally:

- GT20029 could not permeate through skin owing to its physical properties and its blood level is undetectable while applied on the skin of the animals. Thus devoid of any mechanism based side effect.
- GT20029 shows potential in degrading mutant AR protein which will benefit the post AR antagonist treated patient.
- Since the protein will take time to regenerated once it is depleted, the treatment could last longer than antagonist.
- By circumventing the oral bioavailability problem of Protac molecule and pinpoint the effect protein degradation, this molecule has the potential to prove, for the first time, the effectiveness of Protac technology in drug discovery.

# 6 Clinical Trials of GT20029

## Phase I Clinical Trial in China CTR20211363

Completed first batch of subjects enrollment and dosing on July 28, 2021

### Trial Design

A randomized, double-blind, placebo-controlled phase I trial to evaluate the safety and pharmacokinetic profile of GT20029 gel/tincture in single and multiple topical doses in healthy subjects.

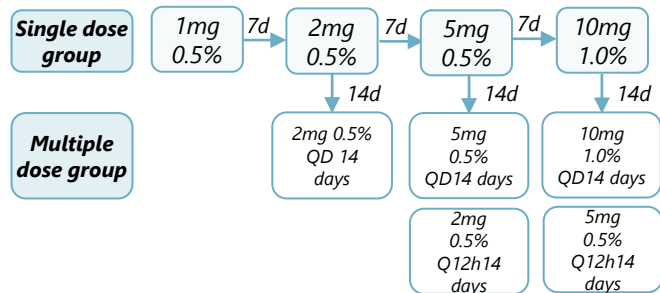
### Subject Recruitment

**Stage 1:** GT20029 gel in single and multiple topical doses (largest subject No. is 68)

Single dose: 4 subjects in 1mg group, 8 subjects in the left groups.

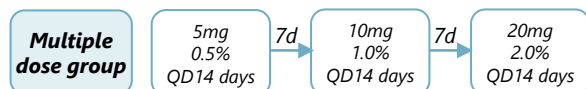
Experimental group: Placebo group=3:1

Multiple doses: 8 subjects/group, Experimental group: Placebo group=3:1



**Stage 2:** GT20029 tincture in multiple topical doses (24 subjects)

Multiple doses: 8 subjects/group, Experimental group: Placebo group=3:1



## Phase I Clinical Trial in the U.S.

Completed first batch of subjects enrollment and dosing on February 1, 2022

### Trial Design

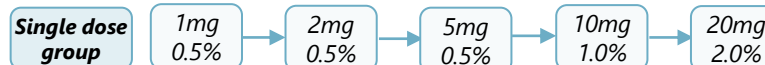
A randomized, double-blind, placebo-controlled Phase I trial to evaluate the safety, tolerability, and pharmacokinetics of GT20029 in subjects with single and multiple ascending doses of topical use.

### Subject Recruitment

**Stage 1:** 40 healthy subjects, single ascending dose, 5 dose groups, 8 subjects/group

Single dose: Experimental group: Placebo group=3:1

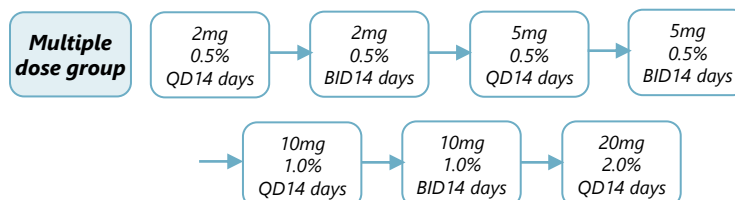
Dose escalation based on safety and tolerability results from previous dose cohort, as determined by PI and medical regulation.



**Stage 2:**

Group A: 56 acne patients, multiple dose escalation, 7 dose groups, 8 people/group

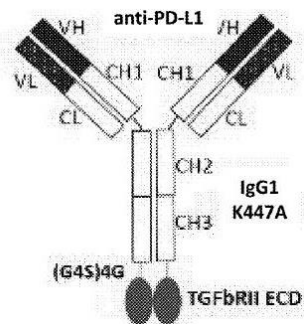
Group B: 56 male AGA patients, multiple dose escalation, 7 dose groups, 8 people/group. Experimental group: Placebo group=3:1





# 7 PD-L1 / TGF- $\beta$ Dual Targeting Antibody

## Advantage in Composition



With a high activity in **inhibiting both PD-L1 and TGF- $\beta$** .

Genetic engineering modification could reduce its degradation or fragmentation in CHO cell expression proteins, which makes it easier to be commercially produced and becomes a **potential "best-in-class" drug**

## Potential Indications and Market Opportunities

Could be treatment for a variety of solid tumours, including:



### Non-small cell lung cancer (NSCLC) 1L/2L

Lung cancer is one of the malignant tumors with the highest incidence and number of deaths. Among them, NSCLC accounts for more than 85%



### Biliary tract cancer (BTC) 1L/2L

From 2019 to 2023, the CAGR of the global BTC treatment market will be close to 6%



### Cervical cancer (CC) 2L

CC ranks the second in mortality rate of cancers among women. About 500,000 women are newly diagnosed with cervical cancer every year globally.



### Nasopharyngeal carcinoma (NPC)

NPC is one of the high incidence of malignant tumors in China, and the incidence rate ranks the first among tumors of otolaryngology

Source: Merck KGaA Official Web, CDE, Technavo market research reports, Press Release

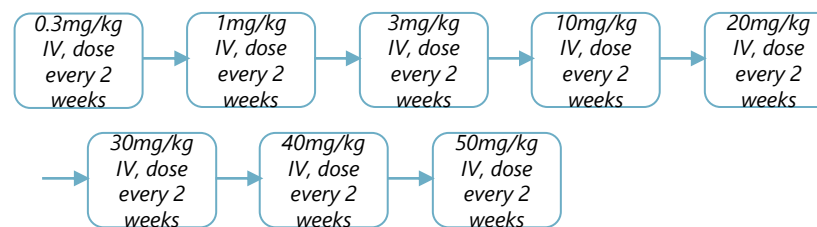
## Phase I Clinical Trial in China

### Trial Design

Phase I trial evaluating the safety, tolerability, pharmacokinetics, and preliminary efficacy of GT90008 in patients with advanced solid tumors.

### Subject Recruitment

#### Dose Escalation Phase (Phase Ia) :3+3 scheme



0.3mg/kg、 1mg/kg、 3mg/kg( 1 patient enrolled) :

- No DLT and no  $\geq 2$  AE - move to next dose group
- DLT occurrence  $\geq 1$  or  $\geq 2$  AE happens -enrollment continues until 3 patients in, then dose following the 3+3 scheme principle

Groups with dosage more than 10mg/kg(enroll 3 patients and follow 3+3 scheme principle) :

- No DLT among 3 patients -move to next dose group
- 1 DLT - 3 more patients should be included
  - No DLT -move to next dose group
  - 1 DLT(2 DLT in total) - move to the next lower dosage group

#### Dose Expansion Phase (Phase Ib)

According to the RP2D in phase Ia, once every two weeks, 28 days is a treatment cycle, 2~4 tumor types are selected, and 20~30 patients are enrolled in each group.



# 8 Detorsertib: mTORC1 and mTORC2 Dual Inhibitor

## Highlights

- ◆ Detorsertib is a second-generation mTOR inhibitor that **inhibits both mTORC1 and mTORC2**
- ◆ Has **shown greater therapeutic advantages** as compared with first-generation mTOR inhibitors that only inhibit mTORC1.
- ◆ There was **no mTORC1/mTORC2 dual inhibitor** that had been approved for marketing globally.

## Global ongoing clinical studies on mTORC1/2 dual inhibitor

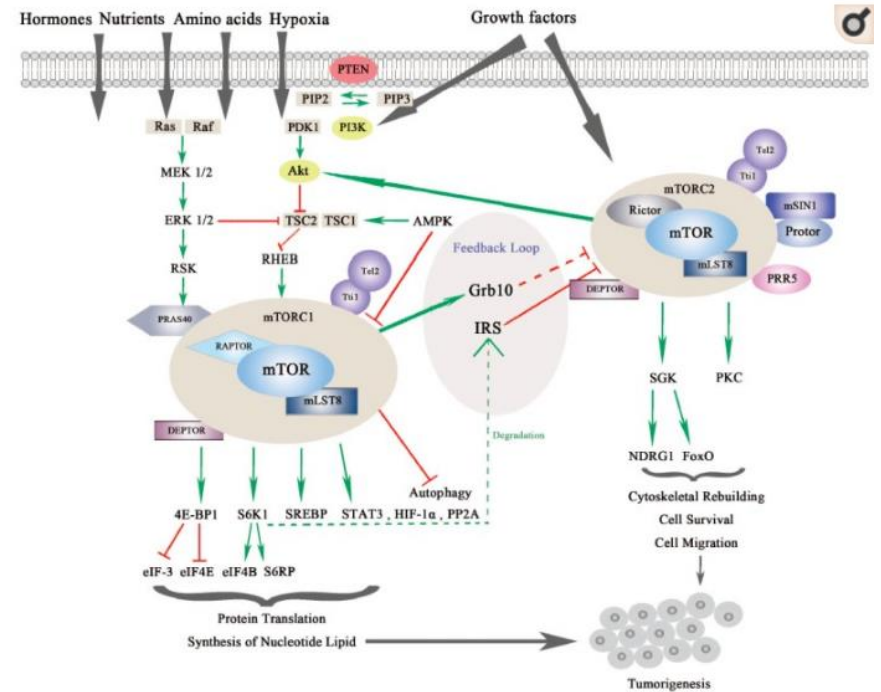
Drugs	Company	Stage/Indications/Locations
Onatasertib (CC-223)	Antengene & Celgene	<ul style="list-style-type: none"> <li>• Phase 2: NSCLC<sup>a</sup>, US</li> <li>• Phase 2: HCC<sup>b</sup>, China/US/S Korea</li> <li>• Phase 2: MM, US</li> <li>• Phase 2: Non-Hodgkin lymphoma, US</li> <li>• Phase 1: Diffuse large B-cell lymphoma, EU/US</li> </ul>
<b>Detorsertib</b>	<b>Kintor</b>	• <b>Phase 1: Leukaemia and BCC, China/US</b>
DFN-529	Diffusion Pharma	• Phase 1: Age related macular degeneration, US
XP-105	Xynomic	• Phase 1: Solid tumor, Germany/Belgium/Italy
SCC-31	Shandong Luoxin	• Phase 1: Metastatic breast cancer

a. CC-223 combo with Erlotinib or Azacitidine; b. CC-223 mono.

### Other drug candidates are in pre-clinical stage

- CMG-101 (developed by CHA University, S. Korea, treatment for RCC)
- mTOR inhibitor (developed by Nankai University)

## MoA



The **PI3K/AKT/mTOR signalling pathway** helps regulate various cellular functions, including cell proliferation, differentiation, apoptosis and nutrition.



First generation mTOR inhibitor only inhibits mTORC1 and has no efficacy on mTORC2, which can cause the activation of oncogene AKT and AMPK and drug resistance through mTORC2.



Detorsertib can **compete with the catalytic site of mTOR for ATP**, reducing the toxicity of dual inhibition of PI3K/mTOR without affecting the feedback pathway such as AKT.



Source: Zhang et al, Int J Mol Sci, 2019, prospectus

# 9 GT1708F: Hedgehog Signaling Pathway SMO Inhibitor

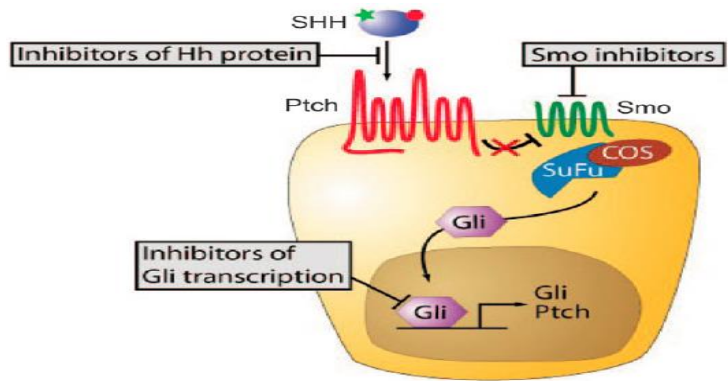
## MoA

Tumour cells have abnormal activation of Hedgehog signalling pathway (PTCH, the patched, deletion or SMO overexpression) and overexpression of the target gene.

The occurrence of medulloblastoma and basal-cell carcinoma are associated with abnormal activation of the Hedgehog signalling pathway.

The Hedgehog signalling pathway is activated by up-regulating SMO in acute myeloid leukaemia cells and chronic myeloid leukaemia stem cells

The occurrence of chronic myeloid leukaemia in a mouse model can be reduced through the inhibition of SMO.



## Competitions

Three approved SMO inhibitors in US/EU: **Glasdegib for AML** (Pfizer), **Sonidegib for BCC** (Novartis/Sun), **Vismodegib for BCC** (Genentech/Roche).

### 🏆 Drugs in clinical stage globally

Drug	Active Company	Global Dev.
Glasdegib	Pfizer	• Phase III, China
Sonidegib	Novartis AG; Sun Pharmaceutical Industries Ltd	• Phase 2: Basal cell nevus syndrome, US; Myelofibrosis: Switzerland • Phase 1: Myelodysplastic syndrome: France
Vismodegib	Genentech Inc; Roche Holding AG	• Phase 2: Meningioma / Head and neck tumor, US • Phase 1: Odontogenic tumor, US
patidegib (topical gel)	PellePharm Inc	• Phase 3: Basal cell nevus syndrome, US • Phase 2: BCC, US/UK
NLM-001	Nelum Corp	• Phase 2: Pancreas tumor, US

### 🏆 Kintor ranks the second among clinical trials in China

NO.	Drug Name	Active Company	Dev. in China
1	Glasdegib	Pfizer Inc	AML: Phase III
2	<b>GT-1708F</b>	<b>Kintor Pharmaceutical Ltd</b>	<b>Leukaemia and BCC: Phase I</b>
3	deuterated vismodegib analogs	Hinova Pharmaceuticals Inc	Preclinical
4	hedgehog signaling pathway inhibitors	Simcere Pharmaceutical Group	Preclinical
5	IMP-5471	IMPACT Therapeutics Inc	Preclinical
6	hedgehog pathway inhibitors	Zhejiang Academy of Medical Sciences	Preclinical
7	hedgehog signaling pathway inhibitors	Fudan University	Preclinical



Source: Prospectus



# 10 Integrated R&D Platform Spearheaded By Top Scientists



**Dr. Youzhi Tong**  
Chairman, CEO & Founder

- 25+ years of experience in biopharm R&D and management
- Former VP of Angion Biomedica in the U.S.
- Former Assistant professor of Albert Einstein College of Medicine
- Ph.D. in pharmacology from Cornell; MA and BA in Chemistry from PKU



**Dr. Xunwei Dong (M.D.)**  
Chief Medical Officer

- 18+ years medical related experience in Novartis, Pfizer and GSK
- Previous Clinical Development Medical director of Novartis
- 10 years experience as an attending surgeon
- M.D. from Peking Union Medical College



**Dr. Qun Lu**  
Chief Technology Officer

- 20+ years of experience in CMC development in Pfizer, Merck and Celgene Corp./BMS
- Member of the board of directors of International Consortium for Innovation and Quality in Pharmaceutical Development
- Ph.D. in Physical Chemistry at Arizona State University; BA in Chemistry from PKU



**Lucy Lu**  
Chief Financial Officer,  
Joint Company Secretary

- 13+ years of experience in investment banking
- Former head of investment banking and managing director at GF Capital
- Executive director in the Asian healthcare group at UBS
- MA in Finance from Peking University; BA in Finance from Renmin University of China





# 10 Integrated R&D Platform Spearheaded By Top Scientists



**Liandong Ma**  
Vice President,  
Head of Institute of R&D

- Former senior scientist of Eli Lilly
- 20+ years of experience in the development of new oncology drugs, leading and participating in more than 10 oncology drug R&D projects, and bringing 4 drugs to the clinical stage
- MA and BA in medicine from Harbin Medical University



**Dr. Ruo Xu**  
Vice President  
R&D (Chemistry)

- 20+ years of experience in the pharmaceutical industry
- Former Chief Scientist of Schering-Plough, and worked in Merck for more than 15 years
- Responsible for the design and synthesis of more than 7 small molecule inhibitors
- Ph.D. in chemistry from Columbia University; BA in chemistry from Peking University



**Dr. Jianfei Yang**  
Vice President  
R&D (Biologics)

- 17+ years of experience in Boehringer-Ingelheim and GSK in immune-related drug R&D
- Published 12 papers as corresponding authors and holds 4 patents
- Ph.D. in pathology from Niigata University School of Medicine



**Dr. Jiawen Han (M.D.)**  
Vice President  
Business Development

- 25+ years of experience in drug development and business operations
- Former VP of Qilu Boston and Wuxi AppTec Pharmaceutical Inc
- M.D. from Peking University, Ph.D. from University of Rochester School of Medicine



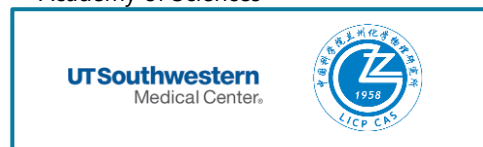
**Juping Shen**  
Deputy General Manager

- 30+ years of experience in the pharmaceutical industry
- Worked in Otsuka, Eisai, Chiatai Tianqing, Sanhome, Fresenius Kabi
- MA from East-South University; BA from Chinese Pharmaceutical University



**Dr. Jie Chen**  
Deputy General Manager

- 10+ years of experience in drug R&D
- Published nearly 20 papers and holds 4 patents
- Working as guest researcher at Suzhou Research Institute of LICP
- Ph.D. in organic chemistry from Chinese Academy of Sciences



**Luke Cheung**  
Vice President  
Investment &  
International Commerce

- 15+ experience in financial and investment
- Former head of Leveraged & Acquisition Finance in Haitong International
- Master of Philosophy, Medical School, the University of Hong Kong; BSc in Biochemistry, the Hong Kong University of Science and Technology



# 11 GMP Facilities and Commercialization

## MANUFACTURING AND R&D BASE

- *c. 20,000 m<sup>2</sup> factory in Suzhou*
- *Put into operation at the end of Aug 2020*
- *Received production permit in 23 Nov 2020, and will obtain China GMP certification, as well as **FDA GMP and EU GMP** subsequently*
- *To meet the commercialization needs of proxalutamide (expect to cover **50 million people** in 2022), and clinical needs of pyrilitamide*



## STRATEGIC COOPERATION AGREEMENT



### PT Etana Biotechnologies

*In Aug 2021, signed the licensing agreement with Etana on the commercialization of proxalutamide for the treatment of COVID-19 in Indonesia. Kintor will receive upfront and milestone payments and economic benefit relating to the sales*



### Shanghai Pharma

*In Dec 2021, signed a strategic cooperation framework agreement with Shanghai Pharma in the new product commercialization*



### Fosun Pharma Development

*In Jul 2021, signed licensing agreement with Fosun on the commercialisation of proxalutamide for COVID-19 in India and 28 African countries. Kintor will receive upfront and milestone payments up to RMB560 million and royalty not less than 50% of total operating profit*



### JD Pharmacy

*In Jun 2020, signed a strategic cooperation framework agreement with JD Pharmacy in the marketing and sales of pyrilitamide*



### Visum Pharma

*In Apr 2021, signed the strategic cooperation agreement with Visum which has strength in production and was certified by US FDA, on expanding the supply capacity of proxalutamide*



### Sinopharm

*In Mar 2020, signed the strategic cooperation agreement with Sinopharm in the market development of pyrilitamide*





Section 3

# Our Strategies

# Our Strategies



*Rapidly advance the clinical development, regulatory approvals and commercial launch of proxalutamide in COVID-19*



*Strategically progress the clinical development of proxalutamide in oncology therapies*



*Continue the phase III/II clinical development of pyrilitamide for the treatment of AGA and acne in both China and the United States*



*Continue the clinical development of ALK-1 as a monotherapy and combination therapy and increase our focus on biologics R&D*



*Enhance our proprietary R&D capabilities to further the development of potential first-in-class and best-in-class drugs, particularly based on our PROTAC technology platform*



*Explore potential strategic partnerships with global pharmaceutical companies through licensing-in / licensing-out and co-development strategy*





Section 4

# Financial Performance

# Income Statement(Adjusted)

	Year ended 31 December	
	2020	2021
<i>RMB'000</i>		
<b>Revenue</b>	-	<b>34,231</b>
Cost of Sales	-	-
<b>Gross Profit</b>	-	<b>34,231</b>
Other Income	25,134	29,311
Marketing Costs	(8,628)	(14,698)
include: Share Incentive Scheme expenses	-	(5,469)
Administrative Expenses	(77,063)	(103,255)
include: listing cost	(20,761)	-
Share Incentive Scheme expenses	(7,832)	(11,949)
Research and Development Costs	(328,764)	(767,936)
include:Share Incentive Scheme expenses	(20,327)	(19,929)
Other Losses-net/Income-net	(115,530)	(17,254)
<b>Operating Loss</b>	<b>(504,851)</b>	<b>(839,601)</b>
Finance costs – net	(3,377)	(2,494)
<b>Loss before Income Tax</b>	<b>(508,228)</b>	<b>(842,095)</b>
Income tax expense	(73)	-
<b>Total Loss</b>	<b>(508,301)</b>	<b>(842,095)</b>
exclude: one-time expenses and non-cash items	48,920	37,347
<b>Adjusted Total Loss</b>	<b>(459,381)</b>	<b>(804,748)</b>

- Exclude one-time expenses and non-cash items( listing cost and Share Incentive Scheme expenses)
- The listing expenses in 2020 was RMB20.8M (USD3.27M), the equity incentive plan expenses was RMB28.2M (USD4.43M); The equity incentive plan expenses was RMB37.3M (USD5.86M).

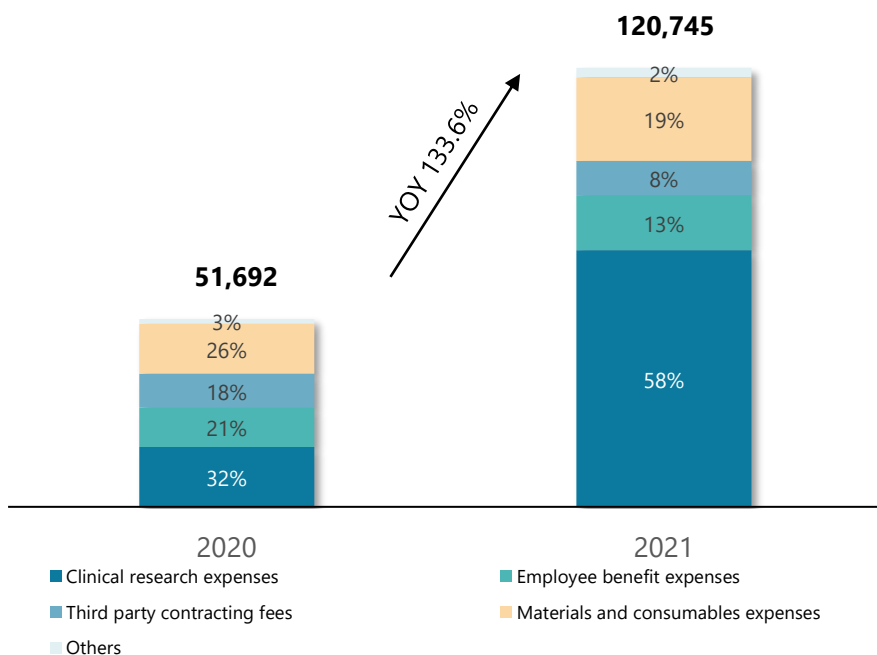


Note: USD/RMB=6.36

# Key Financial Indicators Overview

## R&D Cost

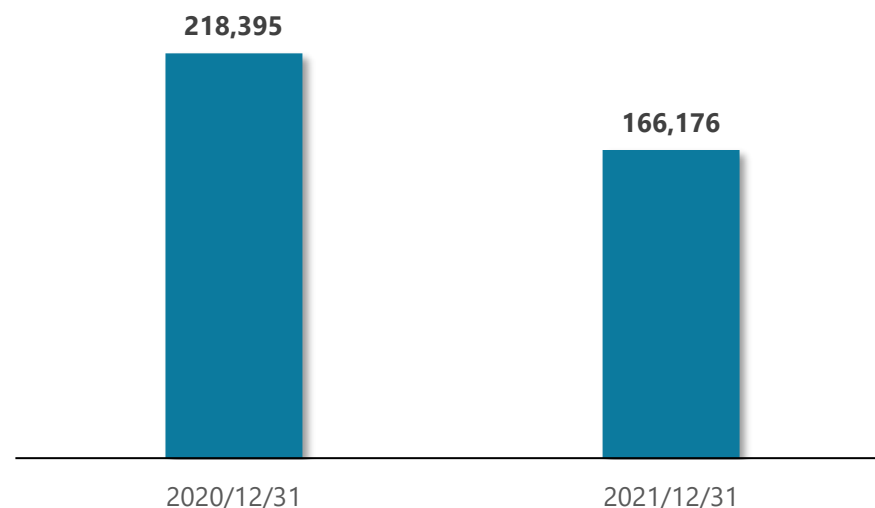
USD'000



- R&D costs increased by 133.6% YoY in 2021, mainly due to: (i) an increase of RMB344.2M (USD54.12M) in clinical research expenses paid to hospitals; (ii) employee benefit expenses increased of RMB27.8M (USD4.37M), including an increase of RMB19.9M (USD3.13M) in share incentive scheme expenses; (iii) Materials and consumables expenses increased of RMB59.0M (USD9.28M)

## Cash and Cash Equivalent

USD'000



- Listed in HKEX in May 2020 with a net proceeds of approximately HK\$1.72 billion (USD221M).
- Completed a top-up placing in May 2021, with a net proceeds of approximately HK\$1.16 billion (USD149M)
- As of December 31, 2021, Kintor had RMB1.06 billion (USD167M) in cash on hand, including bank demand deposits, bank principal-guaranteed deposit products and bank deposits; our used bank borrowing amount was RMB150M (USD24M), and the unused bank credit line was RMB1.5 billion (USD239M).

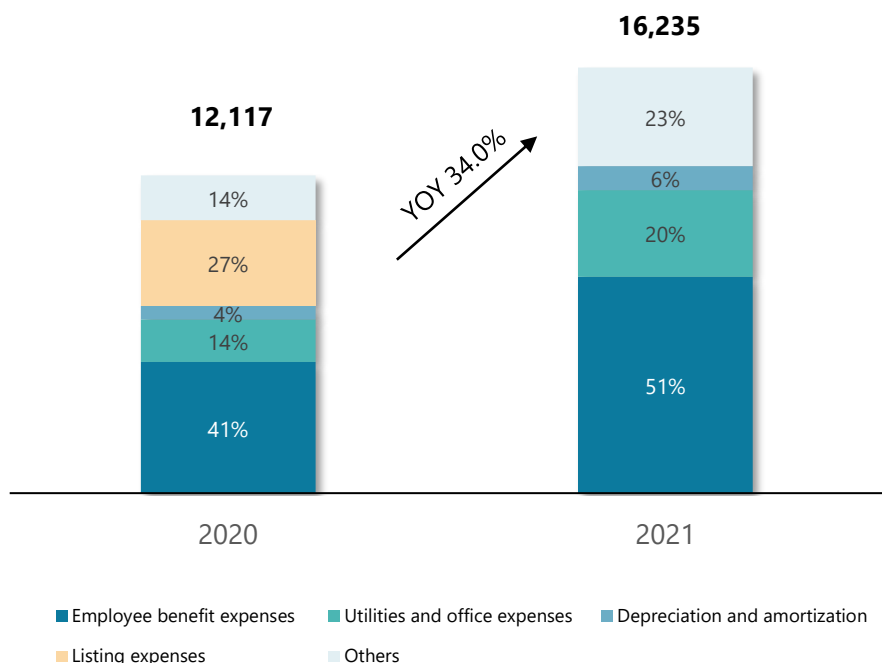


Note: USD/RMB=6.36, USD/HKD=7.8

# Key Financial Indicators Overview(Countinuing)

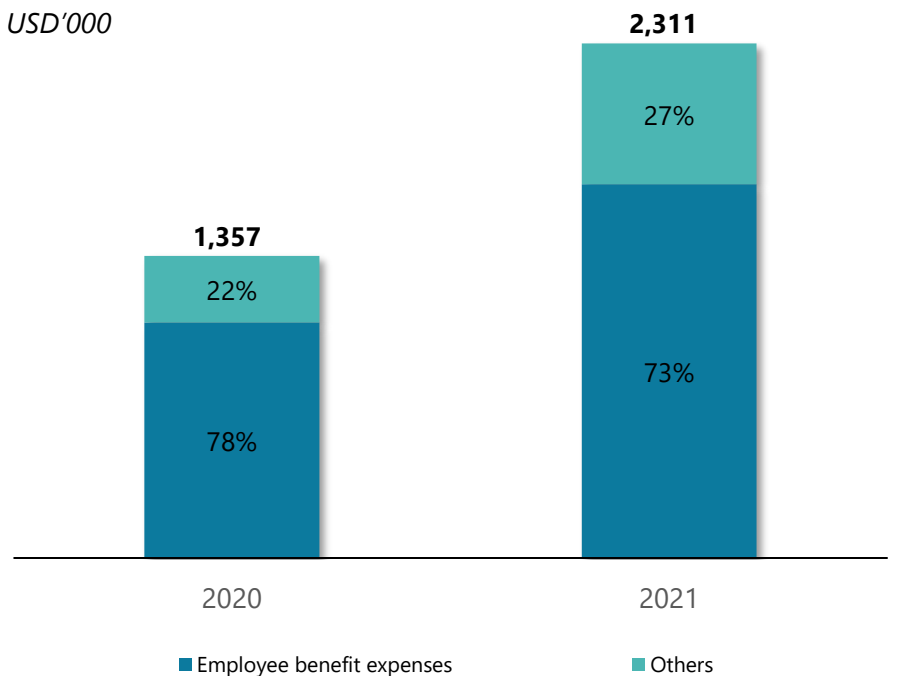
## Administrative Expenses

USD'000



## Marketing Costs

USD'000



- Administrative expenses increased by 34.0% YOY in 2021, mainly due to: (i) employee benefit expenses increased by RMB20.6M (USD3.2M); (ii) office and other general expenses increased by RMB10.7M (USD1.7M) as the office space was expanded; (iii) Listing expenses decreased by RMB20.8M (USD3.3M); (iv) Other administrative expenses increased by RMB13.1M (USD2.1M).

- Distribution and marketing costs increased from RMB8.6M (USD1.4M) in 2020 to RMB14.7M (USD2.3M) in 2021, of which employee benefit expenses increased by RMB3.9M (USD0.6M), mainly due to the establishment and expansion the sales and marketing team preparing for the commercialization of Proxalutamide.



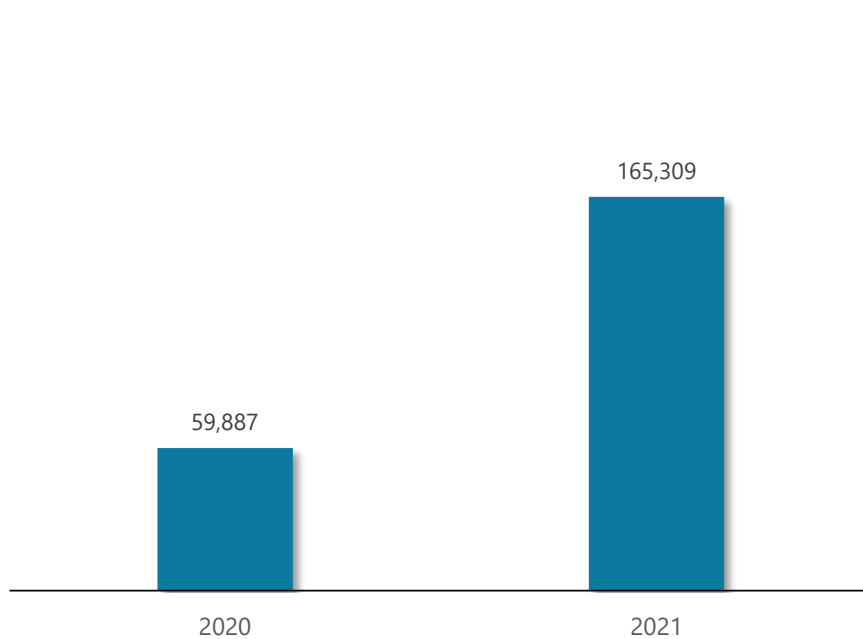
Note: USD/RMB=6.36



# Key Financial Indicators Overview(Countinuing)

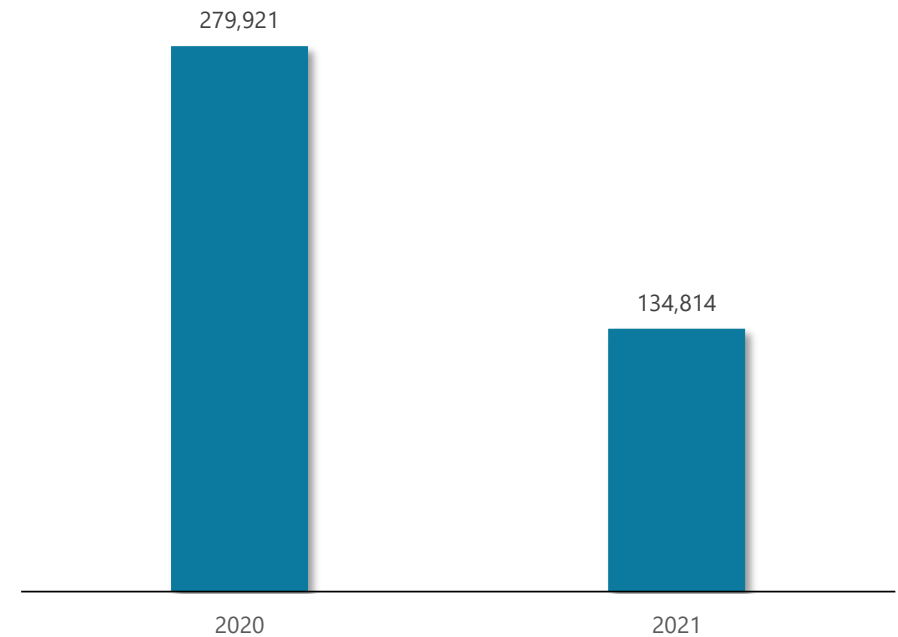
## Net cash outflow from operating activities

USD'000



## Net Cash Flows Generated from Financing Activities

USD'000



- Net cash outflow from operating activities mainly includes R&D expenses and administrative expenses
- The significant YOY increase in R&D expenses in 2021 is mainly due to the increase in the cost of clinical trials for the COVID-19 indication of proxalutamide and the increase in salary and welfare expenses due to the expansion of the R&D team; the increase in administrative expenses is mainly due to the welfare spending increase brought about by non-R&D employee team expansion.

- Net cash inflow from financing activities in 2020 mainly includes IPO proceeds and bank borrowings
- Net cash inflow from financing activities in 2021 mainly comes from the top-up placing.

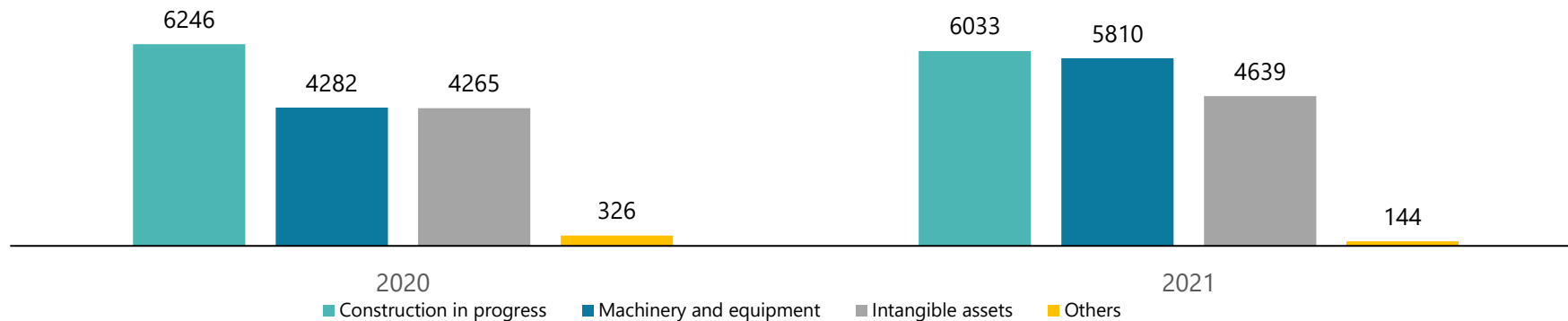


Note: USD/RMB=6.36

# Key Financial Indicators Overview(Countinuing)

## Capital Expenditures

USD'000



- In 2020 and 2021, our capital expenditure amounted to RMB96.2M (USD15.1M) and RMB105.7M (USD16.6M), respectively. The increase was mainly due to the upgrading and transformation of the Suzhou factory to expand its production capacity and the procurement of experimental equipment for Zhuhai R&D Center in Guangdong, etc.
- We expect that the capital expenditure in 2022 will mainly be the design and construction expenditure of the new plant in Pinghu, Zhejiang, etc.



Note: USD/RMB=6.36

# Income Statement

	Year ended 31 December	
	2020	2021
<i>RMB'000</i>		
<b>Income</b>	-	<b>34,231</b>
Cost of Sales	-	-
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Finance costs – net	(3,377)	(2,494)
<b>Loss before Income Tax</b>	<b>(508,228)</b>	<b>(842,095)</b>
Income tax expense	(73)	-
<b>Total Loss</b>	<b>(508,301)</b>	<b>(842,095)</b>

- Our revenue mainly came from license-out income, other income came from interest income and government subsidies, and our main expenses were R&D and administrative expenses
- Among administrative expenses, salary and welfare expenses have increased significantly, and among R&D costs, clinical trial expenses and materials and consumables have increased significantly.
- The clinical trial of COVID-19 indication of Proxalutamide has a large investment in 2021.



# Balance Sheet

	As at 31 December 2020 (Audited)	As at 31 December 2021 (Audited)
<i>RMB'000</i>		
<b>Assets</b>		
<b>Non-current assets</b>		
Property, plant and equipment	174,612	223,686
Intangible assets	209,760	235,621
Right-of-use assets	12,068	38,614
Other non-current assets	34,419	44,173
	<u>430,859</u>	<u>542,094</u>
<b>Current assets</b>		
Inventories	-	351,362
Other receivables, deposits and prepayments	31,621	117,655
Time deposits	323,407	125,071
Restricted cash	-	1,658
Cash and cash equivalents	1,065,588	930,149
	<u>1,420,616</u>	<u>1,525,895</u>
<b>Total assets</b>	<u>1,851,475</u>	<u>2,067,989</u>
<b>Liabilities</b>		
<b>Non-current liabilities</b>		
Borrowings	134,900	147,500
Lease liabilities	490	2,764
Deferred income tax liabilities	38,818	38,818
Deferred income	-	4,009
	<u>174,208</u>	<u>193,091</u>





# Balance Sheet(Countinuing)

	As at 31 December 2020 (Audited)	As at 31 December 2021 (Audited)
<i>RMB'000</i>		
<b>Current liabilities</b>		
Trade and other payables	81,409	209,863
Borrowings	83,600	7,400
Lease liabilities	2,713	2,069
Deferred income	361	-
Amounts due to related parties	1,250	408
	169,333	219,740
<b>Total liabilities</b>	<b>343,541</b>	<b>412,831</b>
<b>Equity</b>		
<b>Equity attributable to the equity holders of the Company</b>		
Share capital	261	273
Shares held for the Employee Incentive Scheme	(17)	(17)
Reserves	1,507,690	1,654,902
<b>Total equity</b>	<b>1,507,934</b>	<b>1,655,158</b>
<b>Total equity and liabilities</b>	<b>1,851,475</b>	<b>2,067,989</b>



# Cash Flow Statement

	As at 31 December	
	2020	2021
<i>RMB'000</i>		
Net cash used in operating activities	(380,882)	(1,051,363)
Net cash generated from/(used in) investing activities	(439,728)	92,005
Net cash generated from financing activities	1780,298	857,418
<b>Net (decrease)/increase in cash and cash equivalents</b>	<b>959,688</b>	<b>(101,940)</b>
Cash and cash equivalents at the beginning of the year	195,532	1,064,689
Exchange losses on cash and cash equivalents	(90,531)	(36,418)
Cash and cash equivalents at the end of the year	<b>1,064,689</b>	<b>926,331</b>



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