

#### **Disclaimer**

This document may contain forward-looking statements that reflect the current views of the Company on future events based on information available as of today's date. Forecasts and estimates are generally identified by words such as "possible", "should", "forecast", "expected", "estimated", "believe", "intend", "plan", "objective" or by the negative form of these expressions or other variations thereof or by the use of comparable terminology.

Although the Company believes that its expectations are based on reasonable assumptions, these forward-looking statements are subject to numerous risks and uncertainties that are beyond Managers' control, including scientific, business, economic and financial factors, which could cause actual results to differ materially from those projected in the forward-looking statements.

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This document does not constitute an offer or invitation to subscribe for or purchase any securities of MolMed S.p.A

The official manager responsible for preparing the Company's financial reports, Salvatore Calabrese, herewith attests, pursuant to Article 154-bis, paragraph 2 of the Legislative Decree 58/1998 ("Testo Unico della Finanza"), that the accounting disclosure contained in this press release matches documentary evidence, corporate books, and accounting records.





- Advanced Therapies scenario
- Company overview
  - Corporate timeline
  - MolMed CDMO competitive positioning
  - MolMed Services and competitive advantages
  - CDMO strategic guidelines
  - Proprietary pipeline
  - Financial highlights



# ATMPs and Cell & Gene Therapy: groundbreaking new opportunities for the treatment of cancer and rare diseases

**Advanced Therapy Medicinal Products (ATMPs)** offer revolutionary innovative opportunities for the long-term management and cure of disease, especially in areas of **high unmet medical need**, creating **transformative**, **one-time durable treatments** and potential cures for some of humankind's most devastating diseases, with the aim to translate promising research into a game changer in healthcare.

Based on the technology used, ATMPs can be classified in:



**Ex-vivo Gene-modified cell therapy**: genetically modify patient/donor cells *ex vivo* (outside the body), which are then introduced into the patient's body in order to fight disease. This approach includes a number of cell-based immunotherapy techniques, such as chimeric antigen receptors (CAR) T therapies and autologous approaches in treating monogenic diseases modifying patient's stem cells.



**In-vivo Gene therapy**: seeks to modify or introduce genes into a patient's body with the goal of durably treating, preventing or potentially even curing disease replacing a mutated gene that causes disease with a functional copy; or introducing a new, correct copy of a gene into the body in order to fight disease.



**Genome Editing**: technique by which DNA is inserted, replaced, removed, or modified at particular locations in the human genome for therapeutic benefit in order to treat cancer, rare inherited disorders, HIV, or other diseases.



**Cell Therapy**: administration of viable, often purified cells into a patient's body to grow, replace, or repair damaged tissue for the treatment of a disease. A variety of different types of cells can be used in cell therapy.



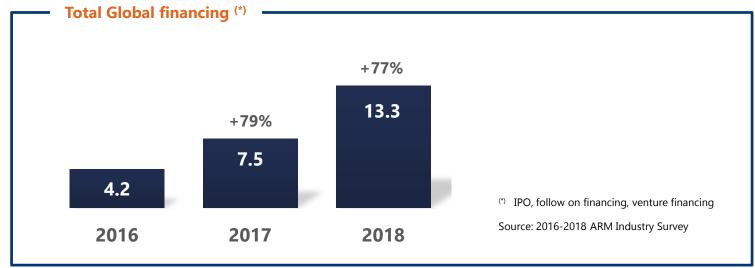
**Tissue Engineering**: restore, maintain, improve, or replace damaged tissues and organs through the combination of scaffolds, cells, and/or biologically active molecules.



# 2016-19, Cell & Gene momentum: major regulatory approvals resulted in an investment surge...

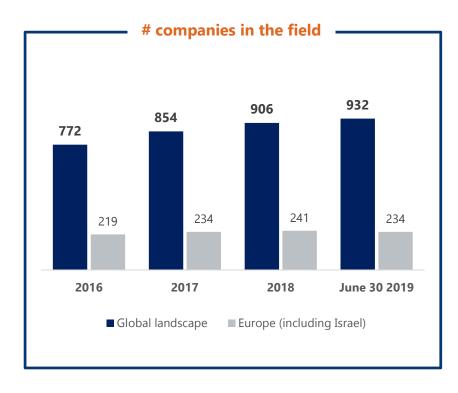
Starting by the end of 2016, after more than 20 years of innovative research, **first FDA and EMA** approvals confirmed the *cost-benefit ratio* of new Cell & Gene therapies.

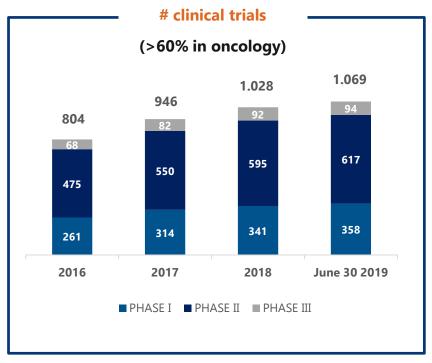






# 2016-19, Cell & Gene momentum: ...increase of companies and clinical trials in the field







# Cell & Gene M&A market 2016-19: big pharmas seek promising new assets to boost their pipelines

#### R&D

#### Gilead to buy Kite Pharma in \$11.9 billion deal

**Aug, 2017** – Gilead Sciences agreed to buy Kite Pharma in a \$11.9 billion deal on Monday, as it looks to fuel growth with an emerging class of cancer immunotherapies that are expected to generate billions. Gilead will pay \$180 per share in an all-cash deal, representing a 29.4% premium over Kite's Friday close. Kite's shares were trading up at \$178.15 before the bell..

# French drugmaker Sanofi is buying biotech company Bioverativ for \$11.6 billion

**Jan, 2018** – French healthcare group Sanofi has agreed to buy U.S. hemophilia specialist Bioverativ for \$11.6 billion, its biggest deal for seven years, which it said would strengthen its presence in treatments for rare diseases.

# Takeda strikes €520M deal to buy cell therapy firm TiGenix

Jan, 2018 – Takeda has put together a €520 million (\$627 million) all-cash deal to acquire TiGenix. The takeover will give Takeda full control of Cx601, a stem cell therapy that is closing in on a European approval in Crohn's disease. [..] The buyout represents an 82% premium over TiGenix's closing price prior to news of the deal broke.

# With \$9 Billion Juno Deal, Celgene Doubles Down on Cancer

**Jan, 2018** – Celgene Corp. made one of its largest deals ever with the \$9 billion acquisition of Juno Therapeutics Inc., placing a costly bet on cutting-edge cancer treatments. Celgene will gain research into a novel class of therapies known as CAR-T that use the body's own immune system cells to fight cancer.

#### Novartis buys AveXis in \$8.7 billion gene therapy bet

**Apr, 2018** – Novartis has agreed to buy AveXis for \$8.7 billion. The \$218-per-share cash deal represents a 72% premium to AveXis's 30-day volume-weighted average stock price [..] adding a rare-disease treatment that could reap billions in sales.

# Roche sees glimmer of hope for \$4.3B Spark deal as FTC staff gives thumbs-up

**Oct, 2019** – After an agonizing wait, Roche might finally be looking at an antitrust clearance from U.S. authorities for its proposed \$4.3 billion takeover of Spark Therapeutics. Roche had its eye on Spark's gene therapy platform, especially its hemophilia franchise.



# ATMPs bottleneck: demand for additional manufacturing capacity

#### Manufacturing is the most important barrier in Cell & Gene therapy right now



#### **CAGR 20.0%**

- **□** Viral vector manufacturing market is projected to reach USD \$815.8M by 2023 from USD \$327.8M in 2018<sup>(\*)</sup>, at a CAGR of 20.0%.
- With 11 genetically modified therapies currently on the market, additional products coming to market for indications with larger patient populations, and 1,069 clinical trial underway worldwide by the end of IH19, are driving this significant increase in demand



(\*) "Source: Viral Vector Manufacturing Market"; MarketsandMarkets research, Aug 2018

#### Companies are looking to address this issue with:

- ✓ a combination of in-house and outsourced approaches
- building out their own manufacturing
- booking manufacturing slots with contract development and manufacturing organizations (CDMOs) and contract manufacturing organizations (CMOs).



# Pace of deal-making in the field highlights gene therapy manufacturers as prime deal targets in 2019

#### **Cells engineering**

# Lonza Acquires Cell and Gene Contract Manufacturer PharmaCell

medical plane and another than

May, 2017 – Lonza successfully completed the acquisition of PharmaCell, one of the most-respected cell and gene contract manufacturers in Europe [...] for EUR 31 million. [...] Pharmacell had sales of EUR 11 million.

# **Hitachi Chemical Agrees \$75M Deal for Caladrius Cell Therapy Manufacturer, PCT**

Mar, 2017 – [...] Hitachi Chemical has agreed to pay Caladrius \$75 million in cash to acquire PCT outright and potentially another \$5 million on the achievement by PCT of certain revenue-based milestones.

# Hitachi Chemical Co. Ltd. Completes Acquisition of Apceth Biopharma GmbH

**Apr, 2019** – [...] Hitachi agreed to buy Apceth for roughly **\$86 million**.

#### **Viral Vectors manufacturing**

#### **Catalent to buy Paragon Bioservices for \$1.2 billion**

**May, 2019** — Catalent, Inc. [...] today announced that it has completed the **\$1.2 billion** acquisition of Paragon Bioservices, Inc., a leading viral vector development and manufacturing partner for gene therapies.

# Thermo Fisher to Acquire Brammer Bio for \$1.7B, Expanding Gene Therapy Presence

Mar, 2019 -- Thermo Fisher Scientific has agreed to acquire Brammer Bio for \$1.7 billion cash in a deal designed to increase the buyer's presence in gene therapy with the viral vector contract development and manufacturing organization (CDMO)[...] Brammer Bio is projected to generate \$250 million in revenue this year, and expects to continue to exceed the projected market growth rate of 25% over the mid-term, according to the companies.

#### **Cognate BioServices announces acquisition of Cobra Biologics**

**Nov, 2019** – To be able to copy & paste content to share with others please contact us at subscriptions@peimedia.com to upgrade your subscription to the appropriate licence

- Cell & Gene CDMOs industry is still highly fragmented but increasing demand for viral vectors is driving acquisitions and investments in the area
- □ Investors and companies focus on the manufacturing setup, how scalable the processes are, and what is being done in process development, considering that in Advanced Therapies "*The product is the process and the process is the product*"
- There is consensus among the analysts\* that the pace of acquisition activity will continue in the future.



# MolMed: 20+ years delivering excellence in the Cell & Gene field

#### **CDMO**

- Among the world leaders in **GMP production of retroviral and lentiviral vectors** and **tailor-made services for Cell & Gene therapy projects**, ensuring end-to-end solutions with the highest clinical and commercial standards for ATMP
- With an estabilished client portfolio including international big pharma, biotech companies, no profits and academias, MolMed is performing a **continuous growth from 2.8 €M in 2011 to 24.2 €M revenue in 2018**
- 2 facilities (~5.000 SQM) authorized for GMP development and manufacturing of Cell & Gene therapies for clinical trials and for the market.

#### **Research & Development on CAR pipeline**

- MolMed is developing a therapeutic platform based on **Chimeric Antigen Receptor** (**CAR**), both autologous and allogeneic
- ☐ The most advanced product, **CAR-T CD44v6** is starting human clinical trials in oncohematologic indications (AML and MM). The product is potentially effective also in several epithelial solid tumors.









# MolMed: 20 years journey of VV manufacturing and Cell engineering

#### **Development of biopharmaceuticals**

**Cell & gene therapy services** 

1996-99



Joint venture to provide cell therapy services 2000-07



Evolution of the business model to become a **fully integrated biotech** 

2008-15



- **IPO** (2008)
- Zalmoxis® and NGRhTNF in PhIII
- New facility@OpenZone
- Acquisition of CAR-T project (CAR-CD44v6)

2016-18



- Increase of client pipeline
- OpenZone facility becomes operational

2018-19



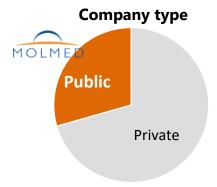
- Consolidated CDMO with yearly growing revenue
- Authorized facilities for clinical and commercial supplies

20+ years as a pioneer in the Cell & Gene field and over 15 years of manufacturing activity makes MolMed an excellence with a solid know-how from basic research to development, manufacturing, clinical validation, regulatory activities and price negotiation of cell & gene therapies.

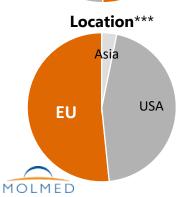


# **MolMed positioning in the CDMO market for Viral Vectors**

# RVV Adenovirus AAV







- ☐ The field of vector CDMOs is accounting for about 50 companies
- MolMed is offering RVV and LVV manufacturing services, the main platforms for *ex-vivo* applications
- ☐ A minority of CDMO is public
- ☐ Most CDMO are similar in size to MolMed or larger
- Notably, >50% of the CDMOs are EU based. In US there are many academic institute that are authorized to support vector demand for clinical PhI/II studies

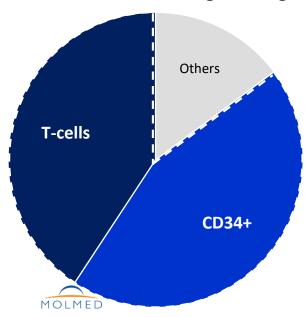
\*not included new vector platforms (i.e. HSV) and non-viral systems
\*\* the employees are not making distinction between
operative/administrative, CDMO vs. pipeline (if present) or VV
personnel vs. other services
\*\*\* location of the head guarter

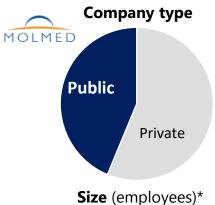
Analysis performed by MolMed Business Development unit

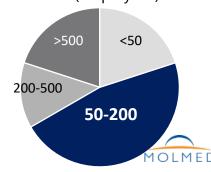


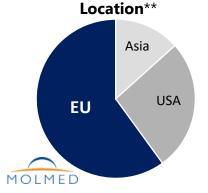
# MolMed positioning in the CDMO market for Genetically Modified Cells

#### **CDMOs for Cell Engineering**









- The field of engineered cells CDMOs is accounting for about 25 companies, about half of the viral vector companies.
- ☐ In the last years, pipeline companies invested a lot in building their own facility for GMP cell-engineering
- MolMed can offer services of gene-engineering in T and CD34+ platforms, matching the current 85% of the offer in this service
- Other platforms are iPSc and mesenchymal cells, with low numbers
- CDMOs offering T-cells and CD34+ ratio is app=1, suggesting that (1) the market is driving the demand on this two services and (2) most of the CDMOs are working on both platforms
- ☐ Cell engineering CDMO are generally smaller in size compared to vector CDMOs

Analysis performed by MolMed Business Development unit



<sup>\*</sup> the employees are not making distinction between operative/administrative, CDMO vs. pipeline (if present) or VV personnel vs. other services

<sup>\*\*</sup> location of the head quarter

# **MolMed's offer: Manufacturing of Viral Vectors and Modified Cells**

#### **Viral Vector GMP Manufacturing**



- ☐ Customization, development, qualification and validation activities carried out by top level Expertise
- Able to perform more than 100 analytical tests in-house, resulting in containment of material, costs and release timelines

#### **GMP** (\*) Cell Engineering

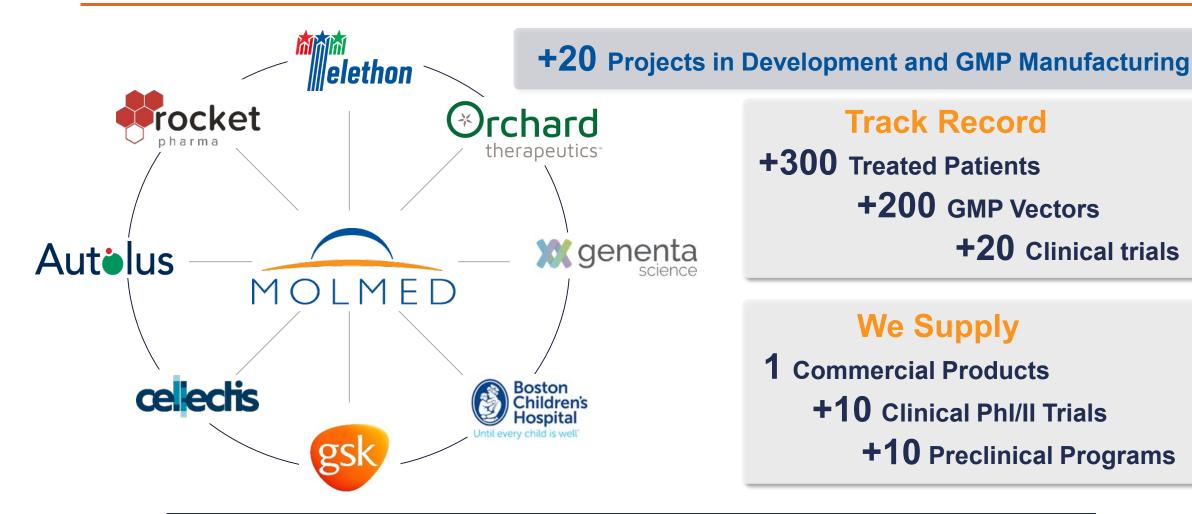
- Top level expertise from tech transfer to fill and finish for clinical and commercial use
- □ Proprietary processes for gene modification of HSC(CD34+) and T-cells, both autologous and allogeneic



MolMed is one of the few players specialized in both Cells Engineering and VV GMP Manufaturing



## **Development and manufacturing partners**



#### **Track Record**

+300 Treated Patients +200 GMP Vectors +20 Clinical trials

# We Supply

**1** Commercial Products +10 Clinical Phl/II Trials +10 Preclinical Programs

#### 8 International Service Partners

March, 9th 2020 15

# **CDMO** strengths

#### **Cell & Gene field**

- ✓ **High demand**: with about 1000 Cell & Gene clinical trials underway in the world at least 50 are expected to arrive on the market by 2030 with a huge increase in demand of VV and engineered Cells
- Entry barriers in C&G manufacturing: complex and resource-intensive processes
- High client retention rate: C&G development & manufacturing agreements have usually a duration of at least 3-5 years, with a complex initial phase of discussions in order to share in depth what has to be the ultimate use of the end product, and the goals needed to produce it. If this process works it usually leads to a strong commitment between client and manufacturer.

#### **Complete Offer base**

- ✓ MolMed's CDMO offering covers a wide range of services for C&G development and manufacturing and is based on the most required products and services in C&G field:
  - Engineered Cells: CD34+ most used platform in advanced therapy against rare genetic diseases, and T lymphocytes, the platform for oncology products (CAR and TCR)
  - <u>Viral Vectors</u>: leading viral platforms in ex vivo gene editing
- Combined offer of engineered Cells beside Viral Vectors represents a competitive advantage (one supplier for the whole process)
- ✓ MolMed can offer both a complete turnkey customer service (key for start-ups and academics) and the technological transfer of its proprietary process for CD34+ and Tcell transduction

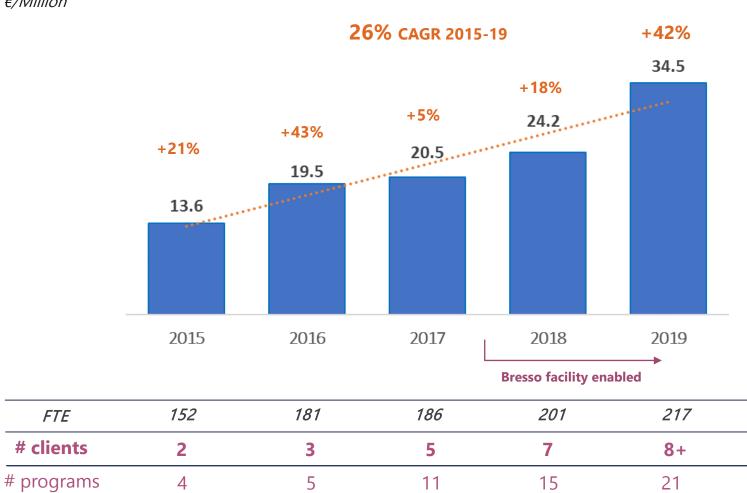
#### **Know-how and Technologies**

- ✓ High level of standardization and processes industrialization
- Most of **QC tests are internalized**, ensuring time optimization and cost reduction
- Optimization of **analytical systems**, with standard platforms already qualified/validated for clinical purposes
- Ability to guarantee short development / production release times
- Standardized regulatory documents and extensive experience in the interaction with Regulatory Authorities
- High manufacturing planning and **facility management capabilities** ensuring the
  highest level of production capacity
  utilization



# **CDMO's Revenues continuous growth**







# **CDMO** strategic guidelines (short / mid term)

High available GMP manufacturing capacity thanks to recent investments in the new facility, offers high margin of growth.

Current capacity utilization can be estimated around 20-40% for cells and 70-80% for VV.

Increase in capacity utilization will follow the expected increase in demand and will be lead by:

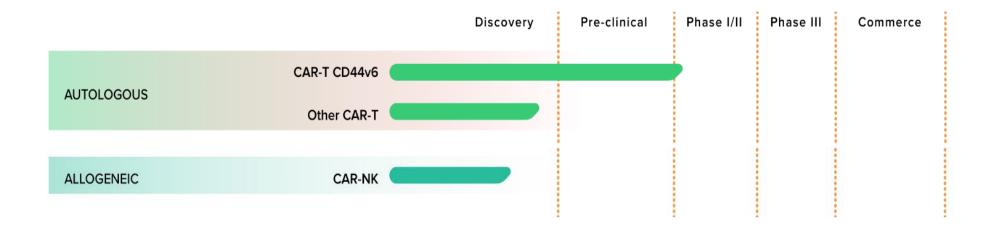
- progressive AIFA regulatory authorization for both VV manufacturing and Cell engineering dedicated
- 7/7 days production
- increase in automation / scale up of manufacturing processes (200+ L LVV bioreactors), allowing higher efficiency and productivity
- increase in Cells programs not requiring additional space
- additional available rooms previously dedicated to Zalmoxis
- → Increase in number of clients
- New services added to MolMed portfolio (i.e. AAV platform, similar to LVV platform, but main platform for in-vivo therapies / on-site injection)



# **Proprietary CAR pipeline**

MolMed's **CAR proprietary pipeline** includes products in different stage, clinical and pre-clinical, both autologous and allogeneic.

- CAR-T CD44v6: in March 2019 received the authorization to start human clinical trials in onco-hematologic indications (AML and MM), following an extensive pre-clinical phase. The product is potentially effective also in several epithelial solid tumors
- CAR NK (Natural Killer): CAR NK cells are one of the most innovative pre-clinical investigations in cellular immunotherapy with much less competition compared to autologous CAR-T. Following a research agreement signed in 2018 with Glycostem, MolMed is developing its own allogeneic CAR NK platform.





# CAR-T CD44v6:

# an original clinical stage therapy, targeting both hematological and solid tumors

MolMed is leading a multi-center, first-in-man Phase I/II clinical trial to demonstrate the safety and the efficacy of CAR-CD44v6 T-cell immunotherapy in:

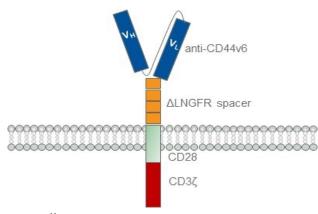
Acute Myeloid Leukemia (AML)

High unmet clinical need

Multiple Myeloma (MM)

#### **CAR-T CD44v6 features**

- ✓ Variant v6 of antigen CD44 is widely expressed in MM and AML
- ✓ **High safety profile** (low skin toxicity and suicide gene)
- ✓ High therapeutic potential in both hematological and solid tumors
- ✓ The **LNGFR spacer** allows selection and *in vivo* tracking of CD44v6 CAR T cells<sup>(\*)</sup>
- ✓ Generation of CD44v6 antigen-loss variants is circumvented by the reduced growth of CD44v6 negative tumor cells
- **✓ No follower approach** on CD19 or other targets in advanced clinical development by large companies



(\*) In May 2019 the European Patent Office (EPO) informed on the decision to grant the patent EP3194434 entitled "Chimeric Antigen Receptors" related to MolMed's spacer used in CAR T CD44v6



## **CAR-T CD44v6 project: strategy and upcoming milestones**

- Horizon 2020 EURE-CART project: MolMed leads a consortium of nine partners, composed of 6 academic centers, 3 SMEs from 5 EU countries experts in oncology and pioneers in the field of Cell & Gene therapy
  - <u>Project scope</u>: to conduct a multicenter first-in-man Phase I/II clinical trial to **demonstrate the safety and the efficacy of CD44v6 CAR-T in AML and MM**
- **EURE-CART project has been awarded with 5M Euro by EU** within the Horizon 2020/Research and Innovation Framework Programme. The project started on January 1st 2017 and will go on until December 2020
- In March 2019 MolMed has been authorized by AIFA to start the clinical trial in AML and MM with CAR-T CD44v6 in the Italian centers
- 3 centers have obtained the necessaries authorizations from their National Authorities to start clinical trials of phase I/II: two in Italy (IRCCS Ospedale San Raffaele and Ospedale Pediatrico Bambino Gesù ) and one in Czech Republic

#### Phase I - Dose escalation

**Objectives:** Maximum Tolerated Dose and Clinical Activity

**18 Pts** (3 dose levels) **up to 30 Pts** (BOIN Adaptive design)

Not before 2021



#### **Phase II – Dose expansion**

**Objectives:** Confirmation of Clinical Activity and Safety Profile

**14 Pts** (1 Dose level selected in Ph. I) per indication (Simon design)

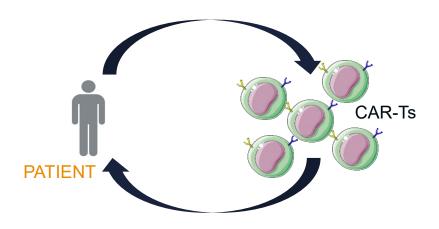
**Basket trial in solid tumors** 

Project scope: delivering a *clinical proof of concept* to license / co-develop the product (no additional investments to complete the clinical phase)



## Allogeneic early stage CAR pipeline

#### **Autologous CAR-T Platform**

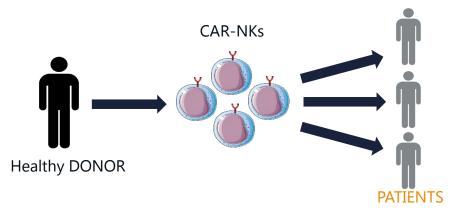


- No GvHD risk
- Proven clinical efficacy
- High production cost (1 batch = 1 patient)



June 28th 2018: **3ys Master Agreement with AbCheck** for the development of new CARs targeting **novel tumor antigens** 

#### **Allogeneic CAR-NK Platform**



- NK cells exclude GvHD
- Lower COGS/patient (significant benefits from both a technical and logistic point of view)
- Wider market potential (1 batch = multiple patients)



May 31<sup>st</sup> 2018: **binding term sheet with Glycostem** for the development and manufacturing of **allogeneic CAR-NK therapies** 

Upcoming milestones: partners and projects assessment by IQ2020



# **Financial highlights: FY 2019**

(Euro thousands)	1		•	
	2019	2018	Change	%
Revenue from CDMO services to third parties	34,338	24,224	+10,114	+42%
Revenue from Zalmoxis®	_	4,223	(4,223)	(100%)
Revenue from sales	34,338	28,447	+5,891	+21%
Other income	1,934	1,433	+501	+35%
Total operating revenues	36,272	29,880	+6,392	+21%
Total operating costs before depreciation and amortization	(32,975)	(32,098)	(877)	+3%
EBITDA	3,297	(2,218)	+5,515	(249%)
Depreciation and amortization	(3,533)	(1,647)	(1,886)	+115%
Totale costi operativi	(32,975)	(33,745)	+770	(2%)
EBIT	(236)	(3,865)	+3,629	(94%)
Net financial income & charges	(105)	(258)	+154	(59%)
Net result before taxes	(341)	(4,123)	+3,783	(92%)
Taxes	(87)	0	(87)	+100%
Net result	(427)	(4,123)	+3,696	(90%)

Molmed has 200 M/€ of NOLs, with a potential deferred tax assets of 50€M that will be reflected in the balance sheets when the Company will be tax profitable.

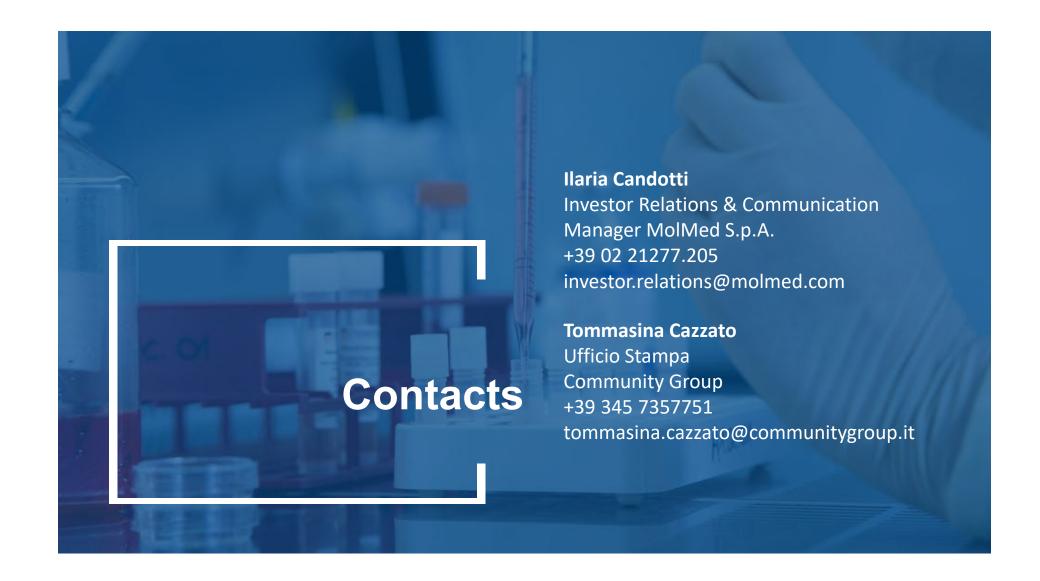


# **Financial highlights: FY 2016-18**

(Euro thousands)	FY 2018	FY 2017	FY 2016	Δ FY18 vs FY17	%	Δ FY17 vs FY16	%
Operating Revenues	29,880	23,987	22,825	5,893	+25%	+1,162	+5%
Revenue from CDMO services to third parties	24,224	20,500	19,484	3,724	+18%	+3,516	+18%
Revenues from Zalmoxis®	4,223	2,500	-	1,723	+69%	2,500	n.a.
Other operating revenues	1,433	987	3,341	446	+45%	(2,354)	(71%)
Operating costs	(33,745)	(32,135)	36,411	(1,610)	+5%	(4,276)	(12%)
Operating Results	(3,865)	(8,148)	(13,586)	+4,283	(53%)	+5,438	+40%
Net Result for the period	(4,123)	(8,497)	(13,876)	+4,374	(51%)	+5,379	+39%
Net Financial Position	16,466	18,111	19,702	(1,645)		(1,591)	
Work Force (#)	201	186	181	+15		+5	

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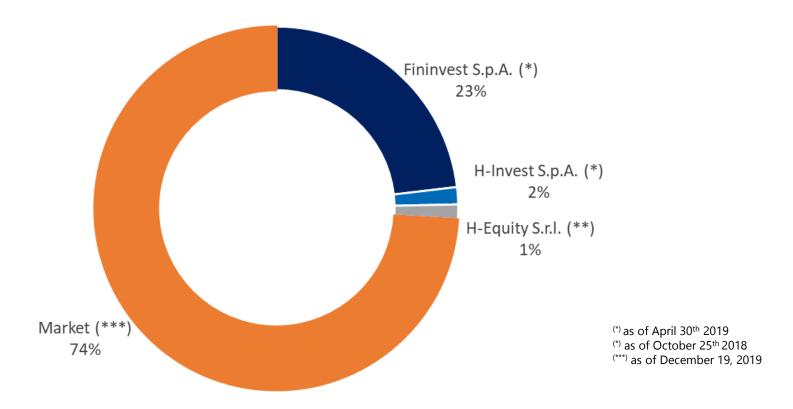


- Shareholders ID
- Executive Management



## **Shareholders ID**

- MolMed is listed on the main market (MTA) of the **Milan Stock Exchange** since 2008 (**MLMD.MI**)
- Market cap ~170M € (as of March, 1<sup>st</sup> 2020)
- **☐** Outstanding shares: 463,450,672





# **Executive Management**



Carlo Incerti, MD - Chairman

- MolMed' Chairman
- Head of Global Medical and Chief Medical Officer Affairs at Sanofi Genzyme (1991-2018)
- Member of the Board of EuropaBio, the European Association for Bioindustries
- Member of the Governing Board of IMI (Innovative Medicine Initiative)









#### Riccardo Palmisano, MD - CEO

- Since 2015 CEO at MolMed S.p.A.
- Since 2016 President of Assobiotec (Italian biotech industries Trade Association)
- Vice President, Managing Director and GM at Genzyme Italy (2005 -15)
- VP Commercial Retail Market at GSK Italy (2003 05)
- Managing Director and GM at Shire Italy (2000 03)



genzyme



FEDERCHIMICA ASSOBIOTEC



**Salvatore Calabrese** - CFO

- Since Sept 2018 CFO at MolMed
- General Manager at Jazz Pharma Italy (2014-18)
- COO and GM at Gentium (NASD) (2005-14)
- Cell Therapeutics Europe (2003-05)
- Manager at PWC (2000-03)



Luca Alberici, PhD, MBA - CBO

- Since 2015 CBO at MolMed
- Bain & Co (2013-15)
- Research Associate at Sanford B. P. Medical Discovery Institute (La Jolla, CA) (2011-12)











