



Calix[n]pyrrole-based anti-cancer compounds

new hope?

prevalence and prognosis of growth of oncological diseases and mortality

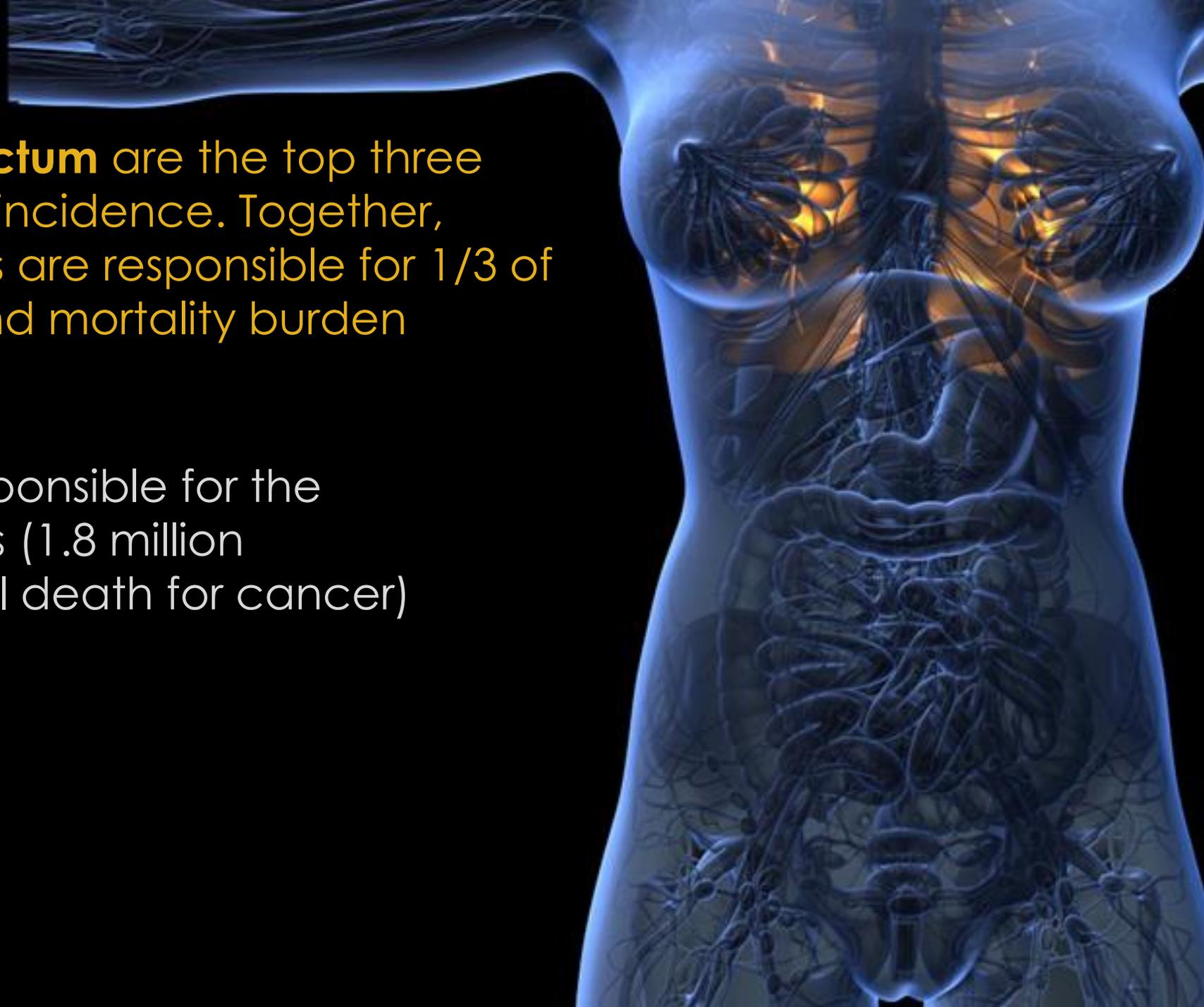
- An estimated **18.1 million new cancer cases** and 9.6 million cancer deaths in 2018*
- Worldwide there will be **27.5 million** new cases of cancer each year by 2040*
- Conventional Chemotherapies: high toxicity, unpalatable side effects
- Modern targeted therapies: used in combination with conventional therapies, often toxic. **Do not meet the cost-effectiveness analysis**
- Current lung cancer standards of care are **inaccurate, risky and expensive**



*World Health Organization, 2018

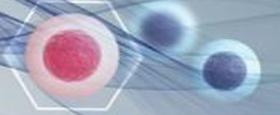
Lung, breast, and colorectum are the top three cancer types in terms of incidence. Together, these three cancer types are responsible for 1/3 of the cancer incidence and mortality burden worldwide.

Lung cancer alone is responsible for the largest number of deaths (1.8 million deaths, 18.4% of the total death for cancer)

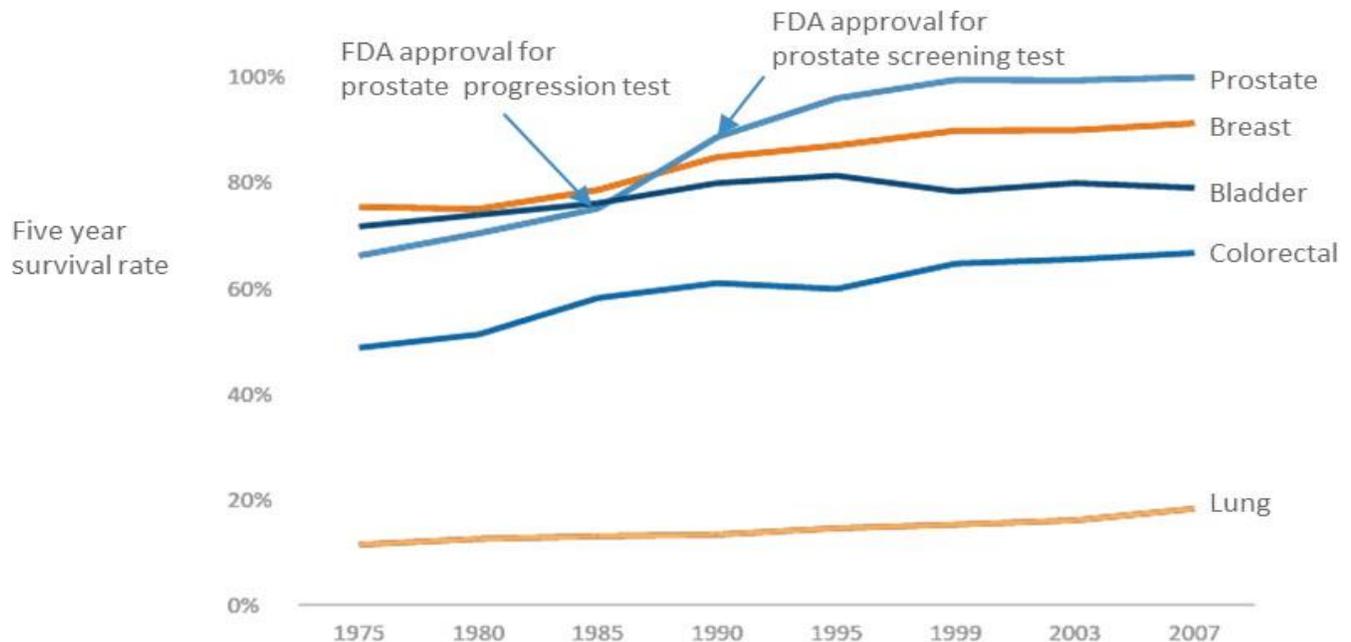




Lung opportunity driven by poor outcomes with little improvement over the last 40 years



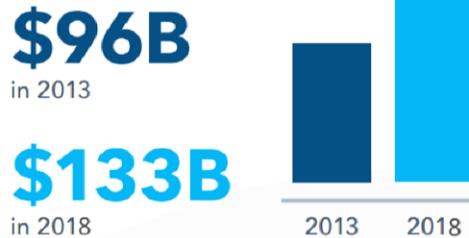
Lung cancer is typically diagnosed at later stages, limiting survival rates
57% of lung cancer diagnoses are made in stage IV



Sources: Cancer SEER Stat Fact Sheets
NCCN Guidelines Lung Cancer Screening 2/2014
USPSTF Screening for Lung Cancer

Antitumor market

 **Rising global spending on cancer medicines**



Rising list prices of new cancer drugs at launch



*U.S. median annual cost

Oncology therapeutic medicines market, 2017-2022

	Average growth	Projected 2022 value
Global Market	10-13%	\$200B
U.S. Market	12-15%	\$100B

Overall, the global market for oncology therapeutic medicines will reach as much as \$200 billion by 2022, averaging 10—13% growth over the next 5 years.*

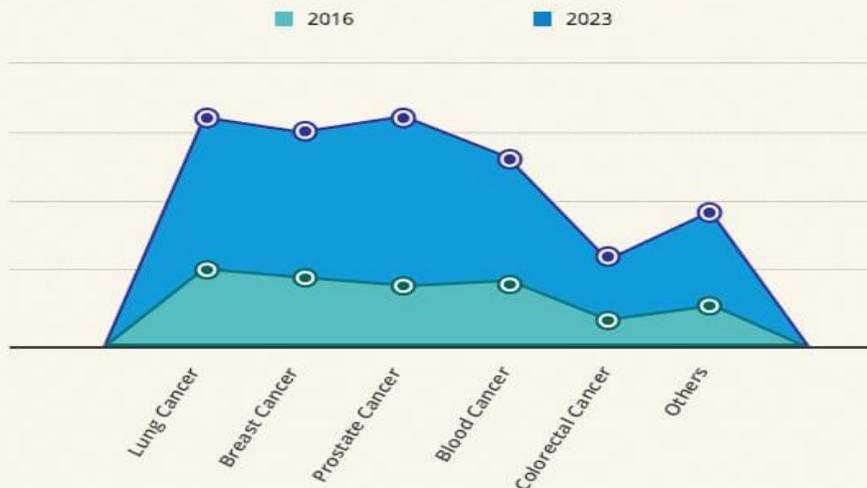
*Sources: <http://www.imshealth.com>, [iqvia institute](http://www.iqvia.com)
<http://www.fda.gov>, <http://www.ema.europa.eu>, <http://www.who.int>



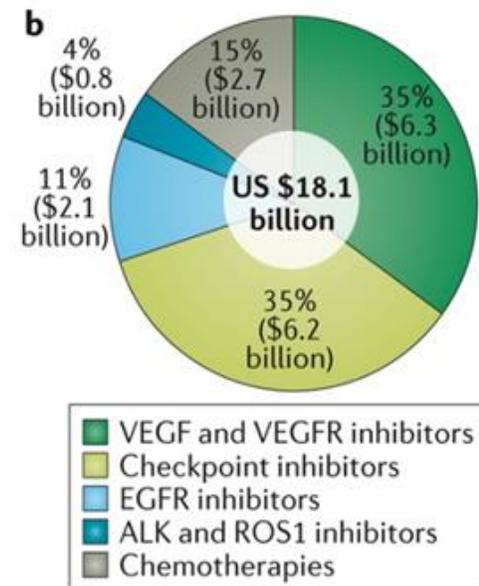
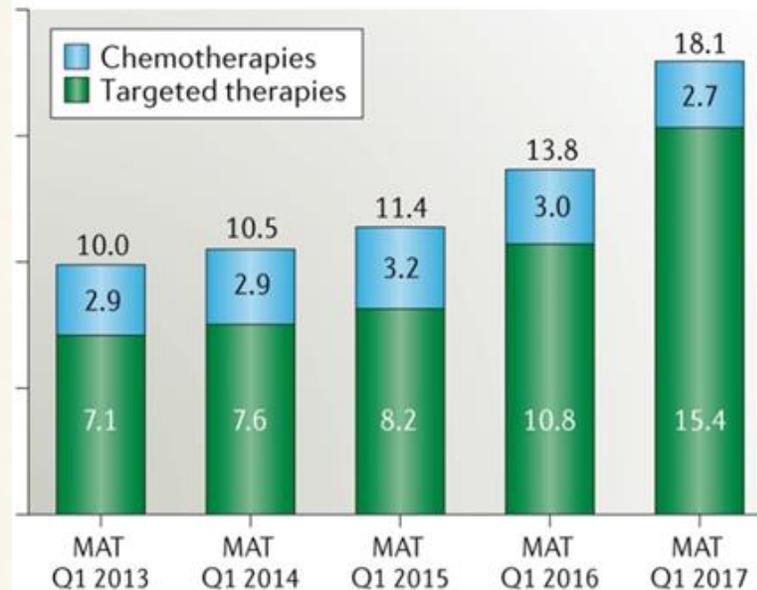
Lung Cancer Market

CANCER THERAPEUTICS MARKET

BY APPLICATION



LUNG CANCER segment occupied the largest market share in 2016.



Nature Reviews | Drug Discovery

The market will be **ACCELERATING** growing at a **CAGR** of about

13%

INCREMENTAL GROWTH

\$ 15.29 bn

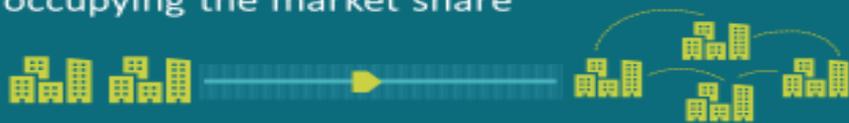
2018

2023

The year-over-year growth rate for **2019** is estimated at

11.86%

The market is **MODERATELY CONCENTRATED** with a few players occupying the market share



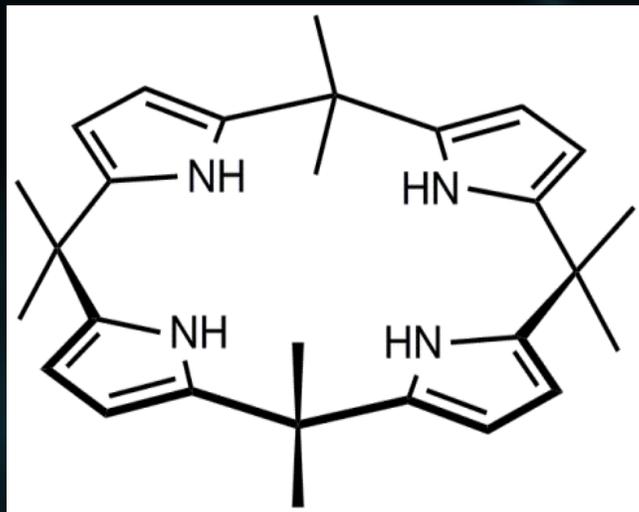
49% of the growth will come from **NORTH AMERICA**



One of the **KEY TRENDS** for this market will be the **ADVENT OF REGENERATIVE THERAPIES**

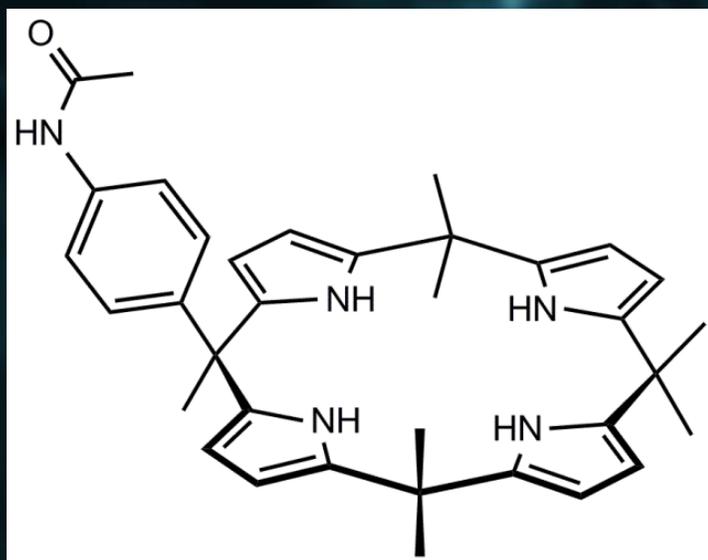


Our Solution: A new class of macrocyclic compounds based on Calix[n]pyrroles

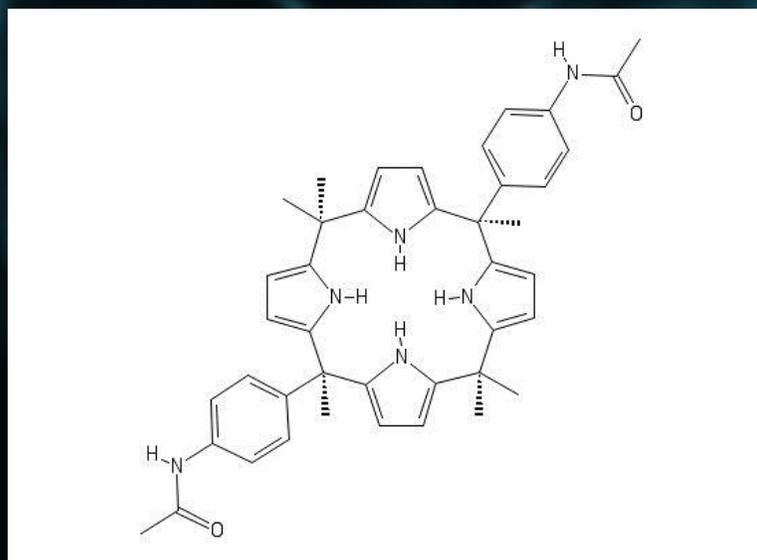


Examples are:

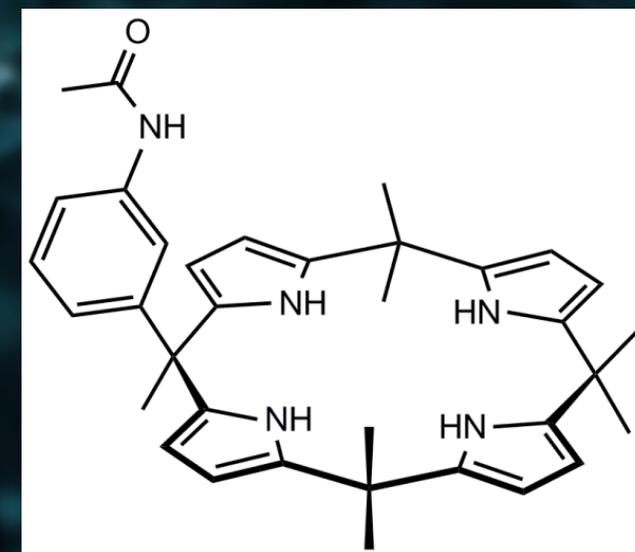
107

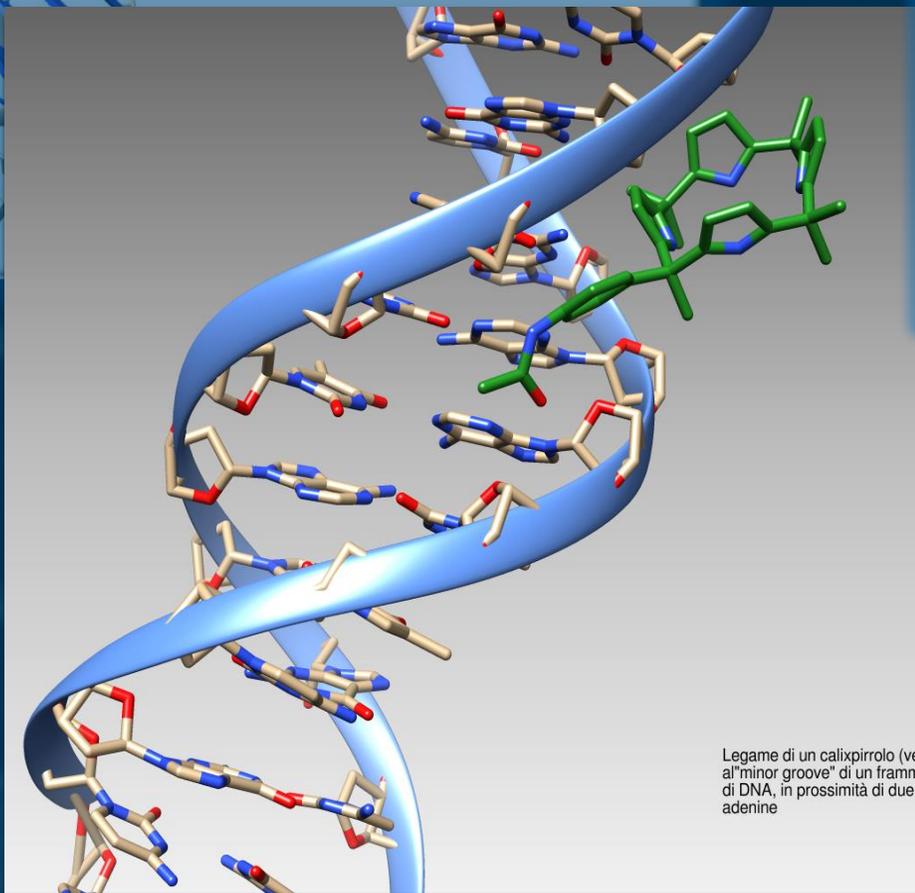


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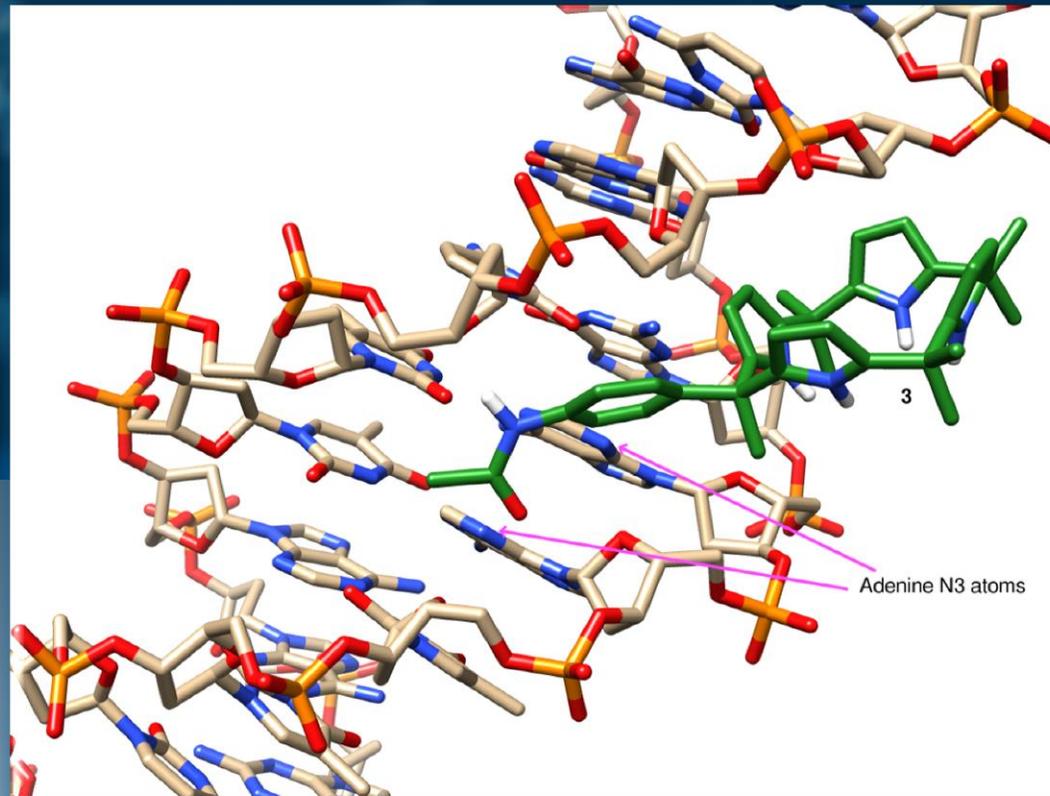


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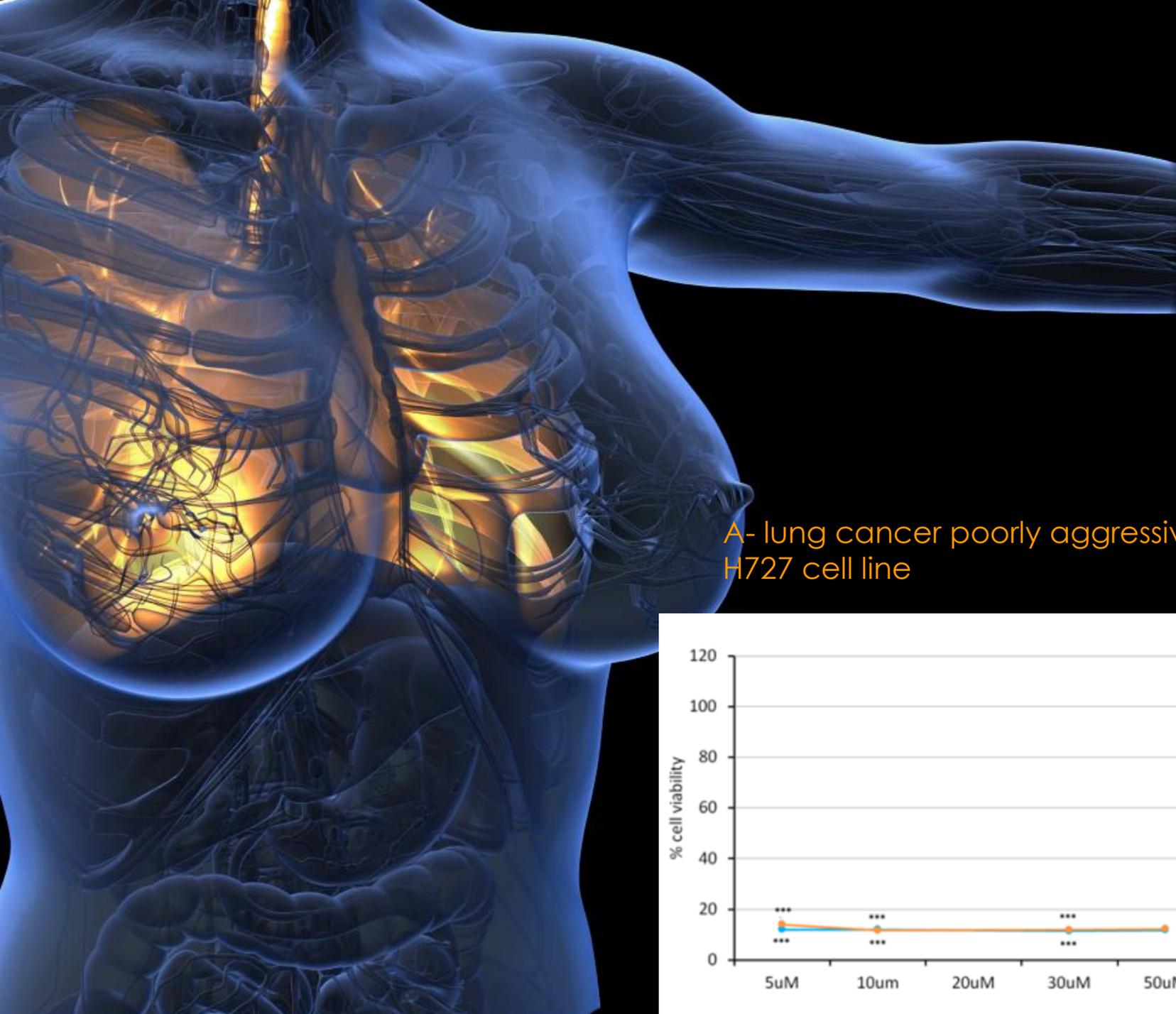


Legame di un calixpirrolo (ve
al "minor groove" di un framme
di DNA, in prossimità di due
adenine



Cytotoxicity of certain calixpyrrole derivatives against specific cancer cell lines.

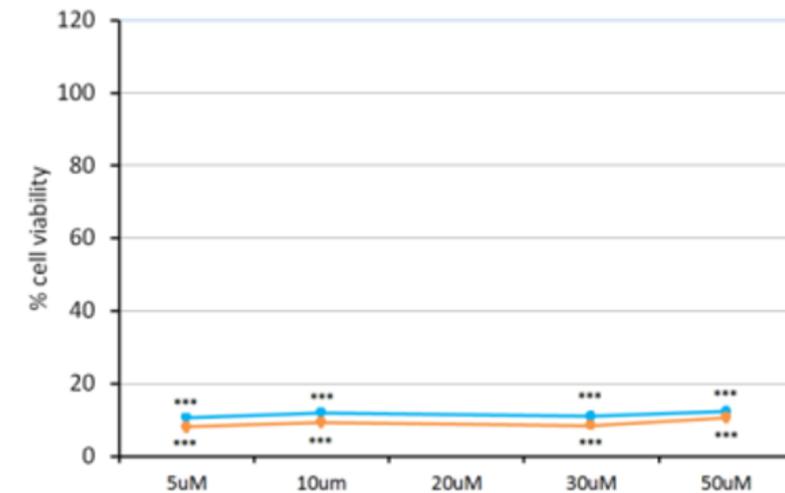
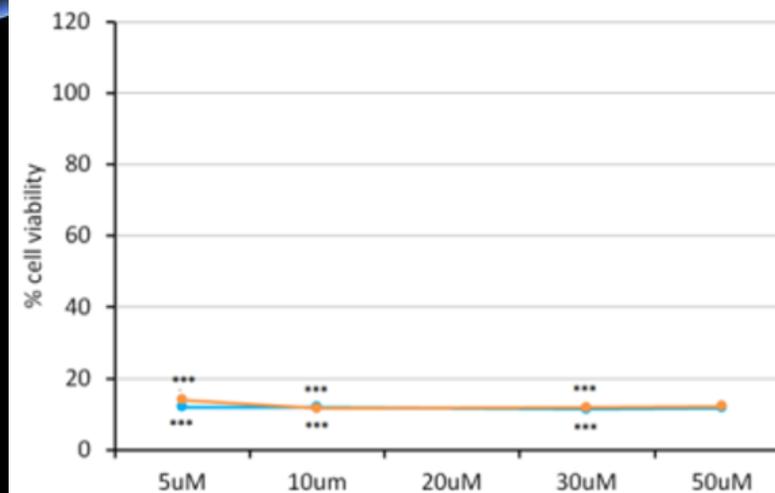
These compounds seem to act via the formation of covalent adducts with DNA, where the genetic damage induces cell death by apoptosis. The formation of covalent adducts was detected using ³²P postlabelling'



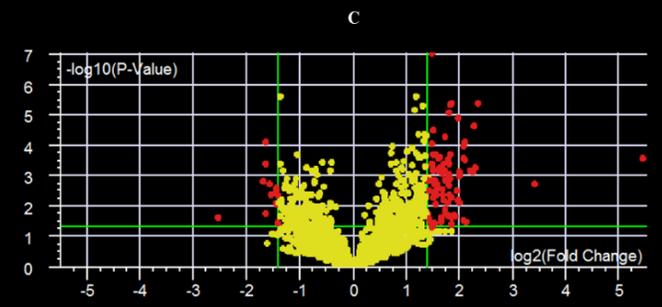
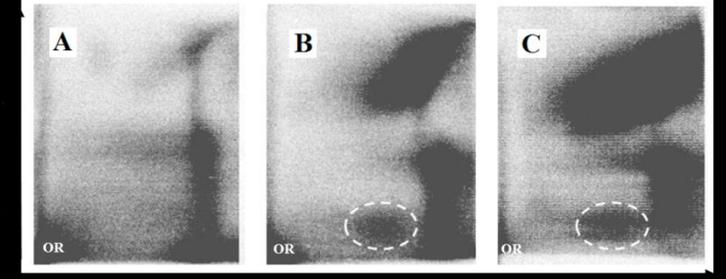
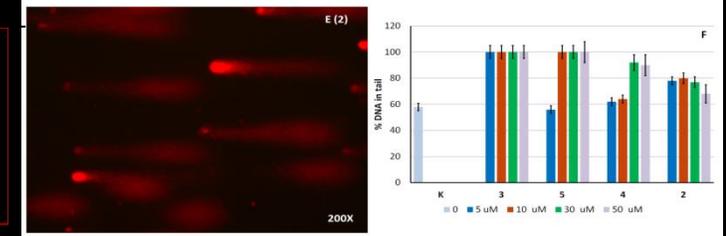
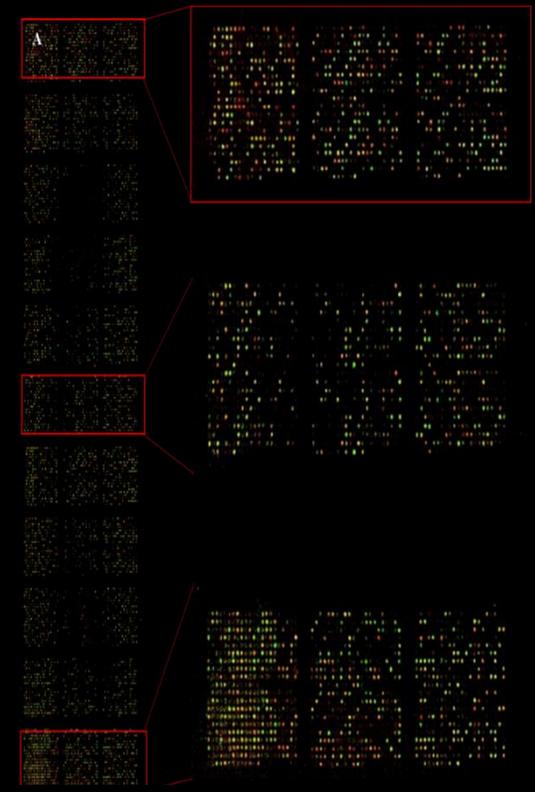
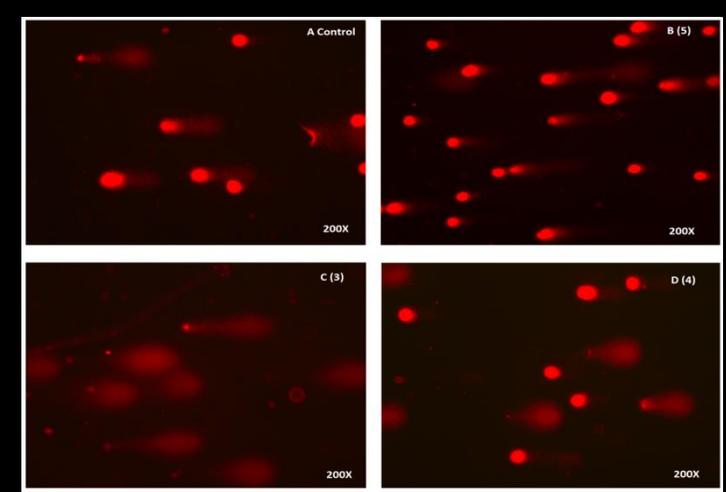
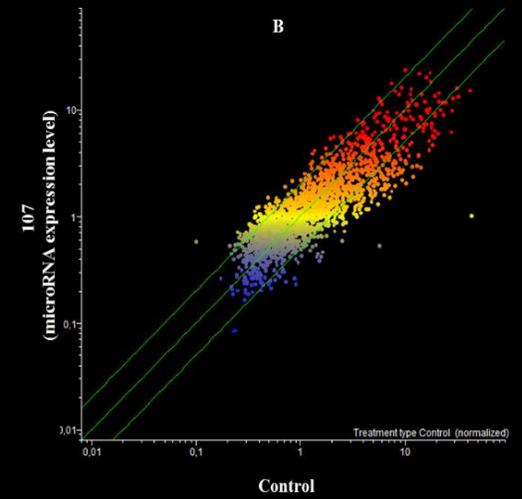
A panel of 12 different cancer cell lines were tested. In the case of Lung cancer A549 and A727, the $EC_{50} < 5\mu M$

A- lung cancer poorly aggressive H727 cell line

B- lung cancer highly aggressive A549 cell line



Our compounds forms DNA adducts, but also induce epigenetic alterations (miRNA)

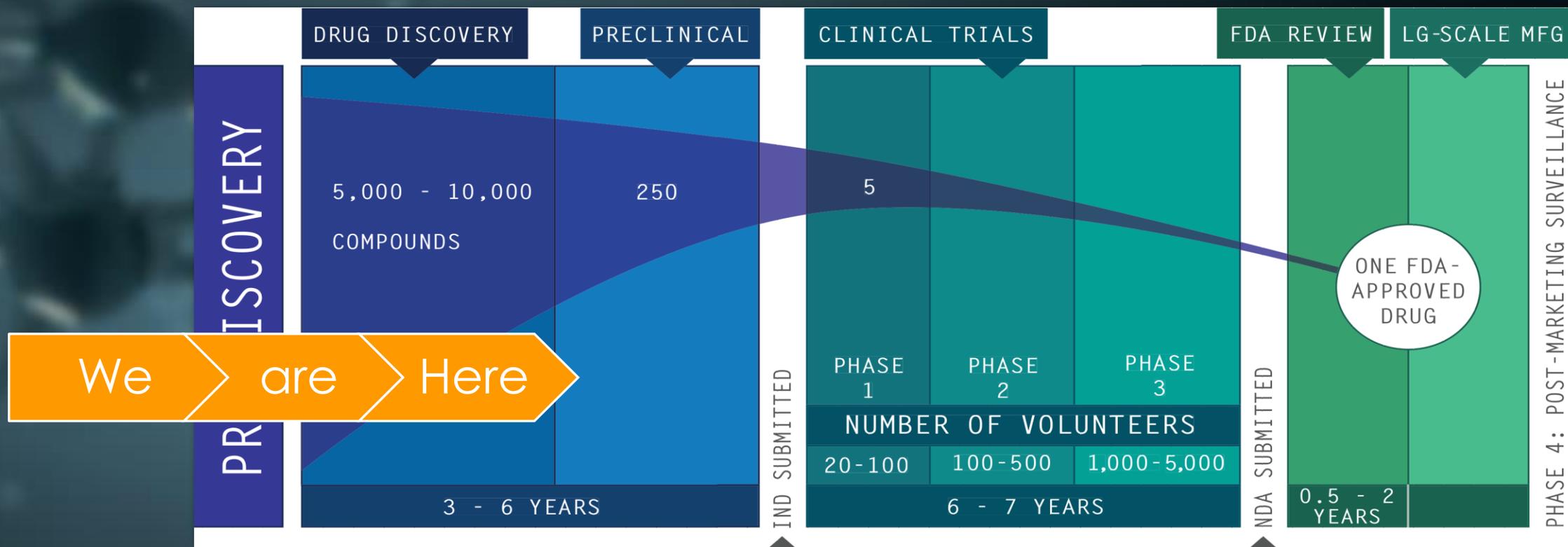


Low toxicity, Brain tumors Brain metastases;



- Preliminary pharmacokinetic tests (A/J mice) showed **107** has extremely **low toxicity** in vivo, even if administered at very high dosage (320mg/Kg). Pharmacodistribution demonstrated its ability to cross the blood-brain barrier.
- **One compound able to hit in one shot, primary tumor and its brain metastases**

Where are we now?



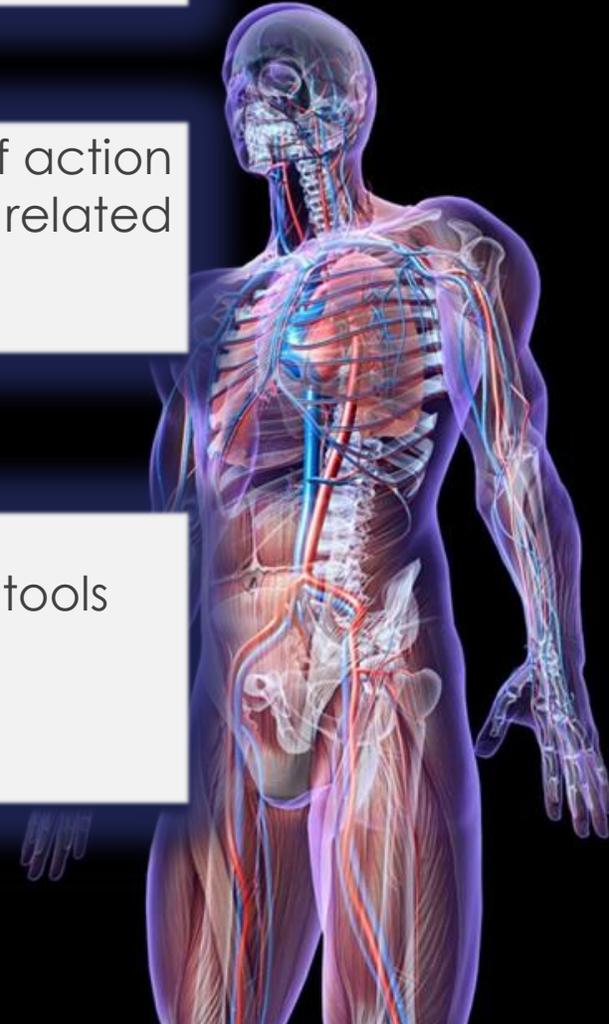
Why do we think we will be here?



► Our patent covers a whole family (cytotoxic) calixpyrroles with **107** and **563** being only two members of the group that we are currently further investigating to become chemiotherapeutic drugs.

► Problems that might arise due to solubility, pharmacokinetics, specificity of action of **107**, and/or **563**, can likely be overcome by the use of other related compounds that are also covered by our patent.

► In fact, we have identified a number of active calixpyrroles and that are characterised by increased solubility, which can be grafted onto delivery tools (including antibodies, dendrimers, polymeric nanoparticles) without any expected loss of activity, but rather achieving augmented selectivity and targeting.



Thank you for your attention! Take a pic, save contacts!

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Anteriority search: negative, freedom to operate.

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