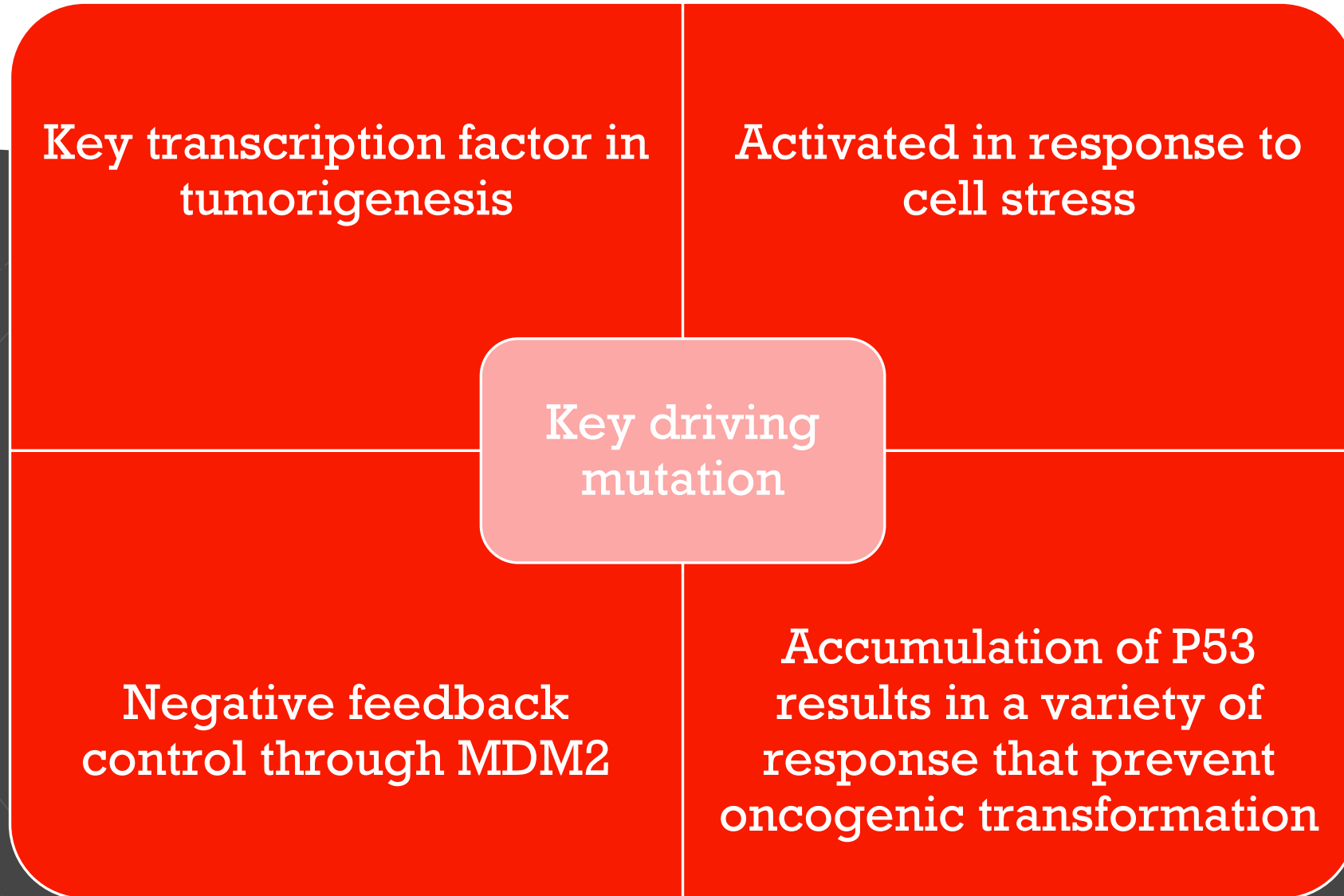


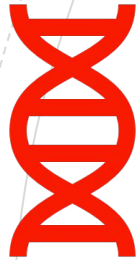
The Potential of P53 Reactivation Therapy



P53 In Cancer



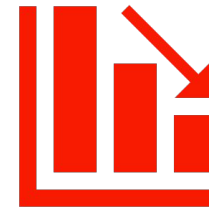
Epidemiology of P53 Mutation



Most frequently altered gene
in human cancer



Exact change varies
between and sometimes with
in tumor types



correlated with increased
resistance to therapy and
poor outcomes

Challenges to Targeting P53



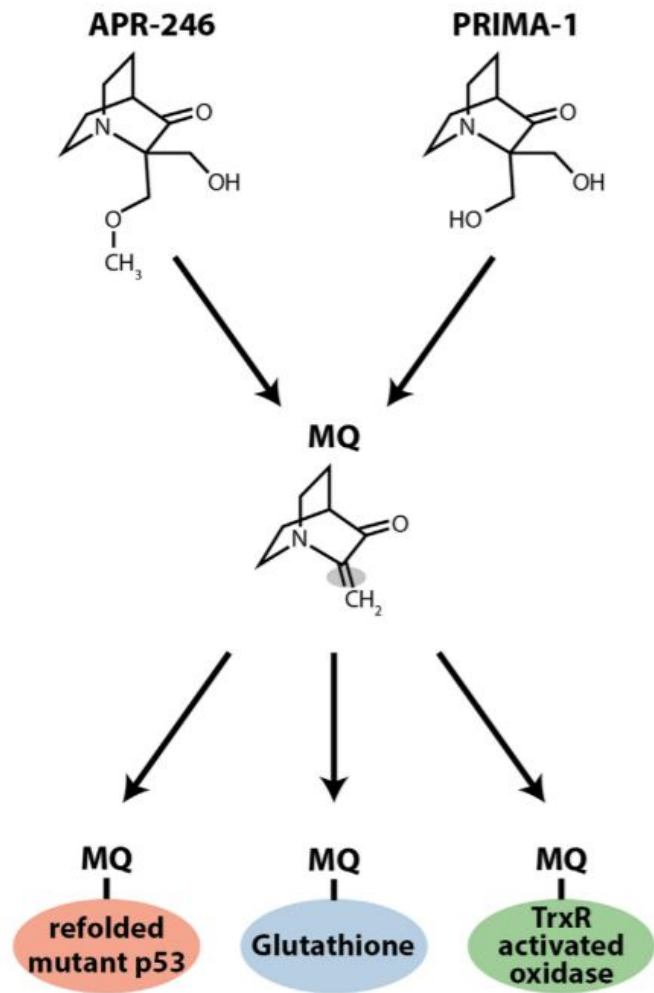
Mutation diversity makes this target very difficult



Each mutation has unique spatial and biological properties

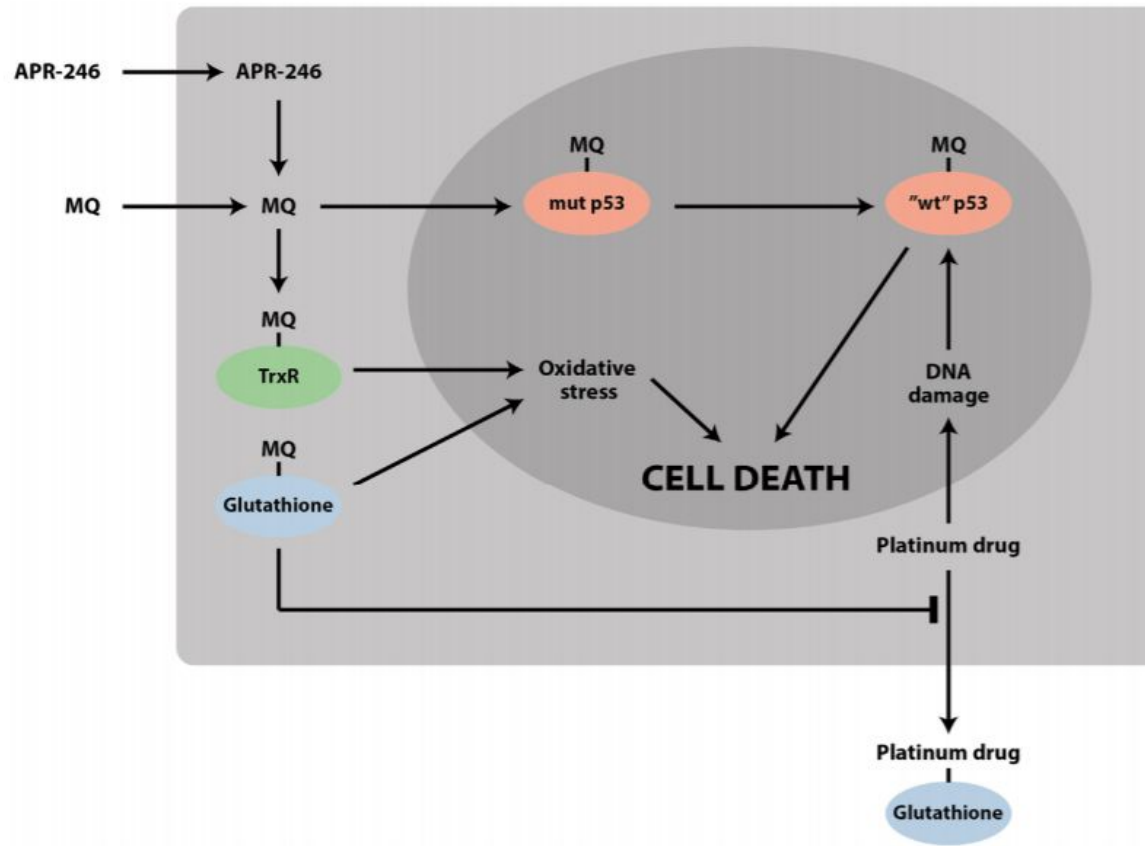


The same tumor may have cells with variations in P53



APR-246 Reactivates P53

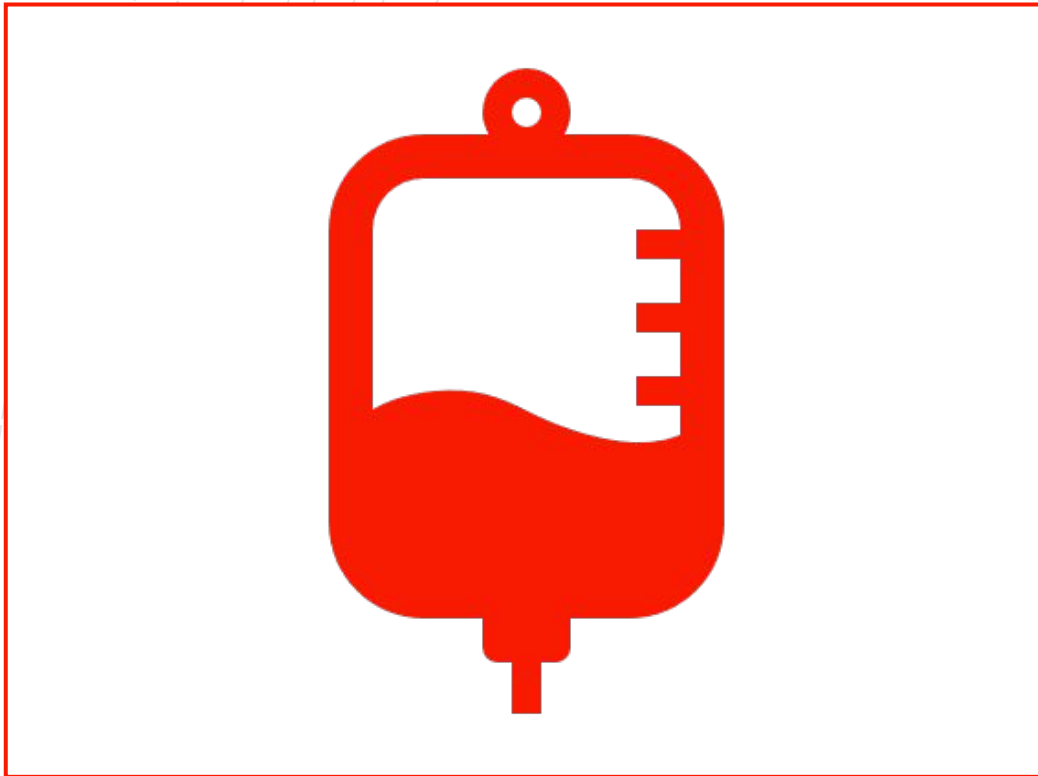
- Prodrug that forms the active compound methylene quinuclidinone (MQ)
- MQ covalently interacts with exposed cysteine residue
- This was in able to induce WT folding
- APR246 will also interact with components of cellular redox system



APR246 Promotes Tumor Sensitization





- Tested in combination with:
 - Imatinib
 - DNA damaging agents (cisplatin, doxorubicin, etc.)

Clinical Data



- **I/IIa Trial in AML**
 - Appears to be well tolerated
 - Patient isolates showed alterations in expression and cell death
- **Ib combination in combination azacytidine in AML**
 - Abstract indicates solo APR has activity and synergy
- **Some data in serious ovarian cancer and breast cancer cell lines**

Clinical Path for APR-246

INDICATION	STAGE OF DEVELOPMENT		
	Phase I	Phase II	Phase III
Myelodysplastic Syndromes (MDS)			
Acute Myeloid Leukemia (AML)			
MDS / AML Post-Transplant Maintenance			
Pending Hematologic Indications			

Granted fast track and orphan drug designation by the FDA

Looking at Some Numbers...

- **AML - Incidence: 3-5 cases/100,000 (16,360 cases in US)**
 - 20% or 3,272 treatable patients
- **High Grade Serous Ovarian Carcinoma**
 - 70-80% of Ovarian neoplasms
 - 225,500 cases/year (WHO est.)
 - 95-100% have P53 mutations
- **Lung Cancer**
 - 234,030 cases/year (ACS est.)
 - 60% have P53 mutations

Why go for AML over other indications?

Aprea



NASDAQ: APRE

Share Price: 30.16

Market Cap: \$633.07M

Recent IPO – Gross Proceeds \$97.75M

High Volatility

Works Cited

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2. Levine A. Targeting Therapies for the p53 Protein in Cancer Treatments. *Annual Review of Cancer Biology* 3:1, 21-34 (2019)
3. Zhang Q, Bykov V, Wiman K et. Al. APR-246 reactivates mutant p53 by targeting cysteines 124 and 277. *Cell Death Dis* 9, 439 (2018)
4. Gourley C, Green J, Gabra H et. Al. PISARRO: A EUTROC phase Ib study of APR-246 in combination with carboplatin (C) and pegylated liposomal doxorubicin (PLD) in platinum sensitive relapsed high grade serous ovarian cancer (HGSOC). *Journal of Clinical Oncology* 2016 34:15_suppl, 5571-5571 (2017)
5. Bykov V, Zhang Q, Zhang M et. Targeting of Mutant p53 and the Cellular Redox Balance by APR-246 as a Strategy for efficient Cancer Therapy. *Front. Oncol.* 6:21.(2016)