

# FIXED DOSE COMBINATION (FDC) PRODUCTS OVERVIEW

Tugrul T. Kararli, Ph.D. MBA

President and Founder

PharmaCircle LLC

# OUTLINE

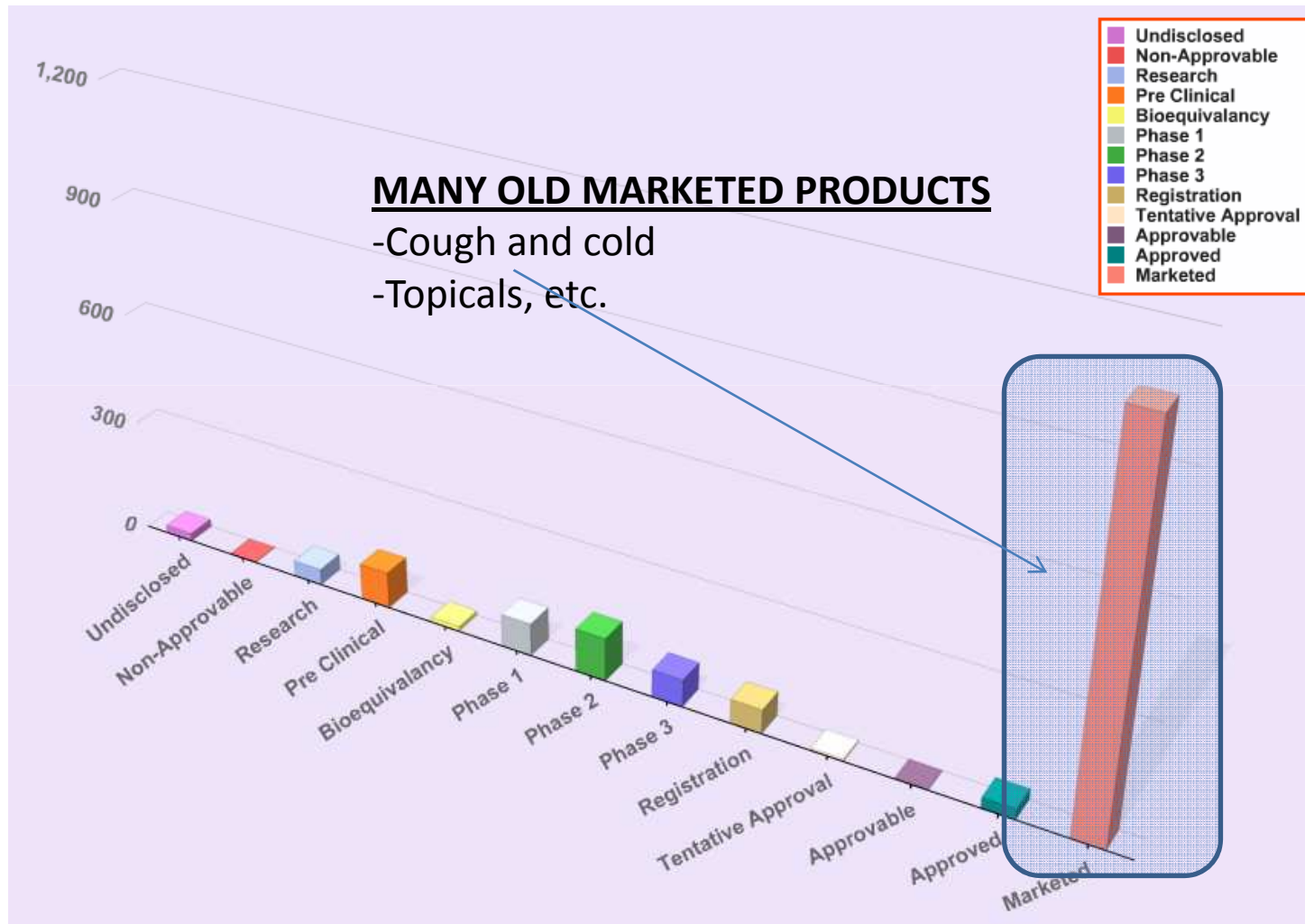
- Rational
- Marketed and Developmental stage FDCs
  - Global picture
  - Large pharma
  - Ther. categories
  - Delivery Routes/DD technologies
- Conclusions

# FIXED DOSE COMBINATIONS (FDC) RATIONAL

- **Improved patient compliance:** Simplified disease management for chronic diseases (e.g. HIV, asthma, diabetes, lipid regulation, hypertension, etc.)
- **Better efficacy:** Synergistic mechanisms, improved ADME & drug resistance
- **Simplified/cost effective handling & distribution** especially for HIV drugs
- **Effective LCM strategy:** New products from proven molecules; patent/market exclusivity, may also combine formulation patent exclusivity

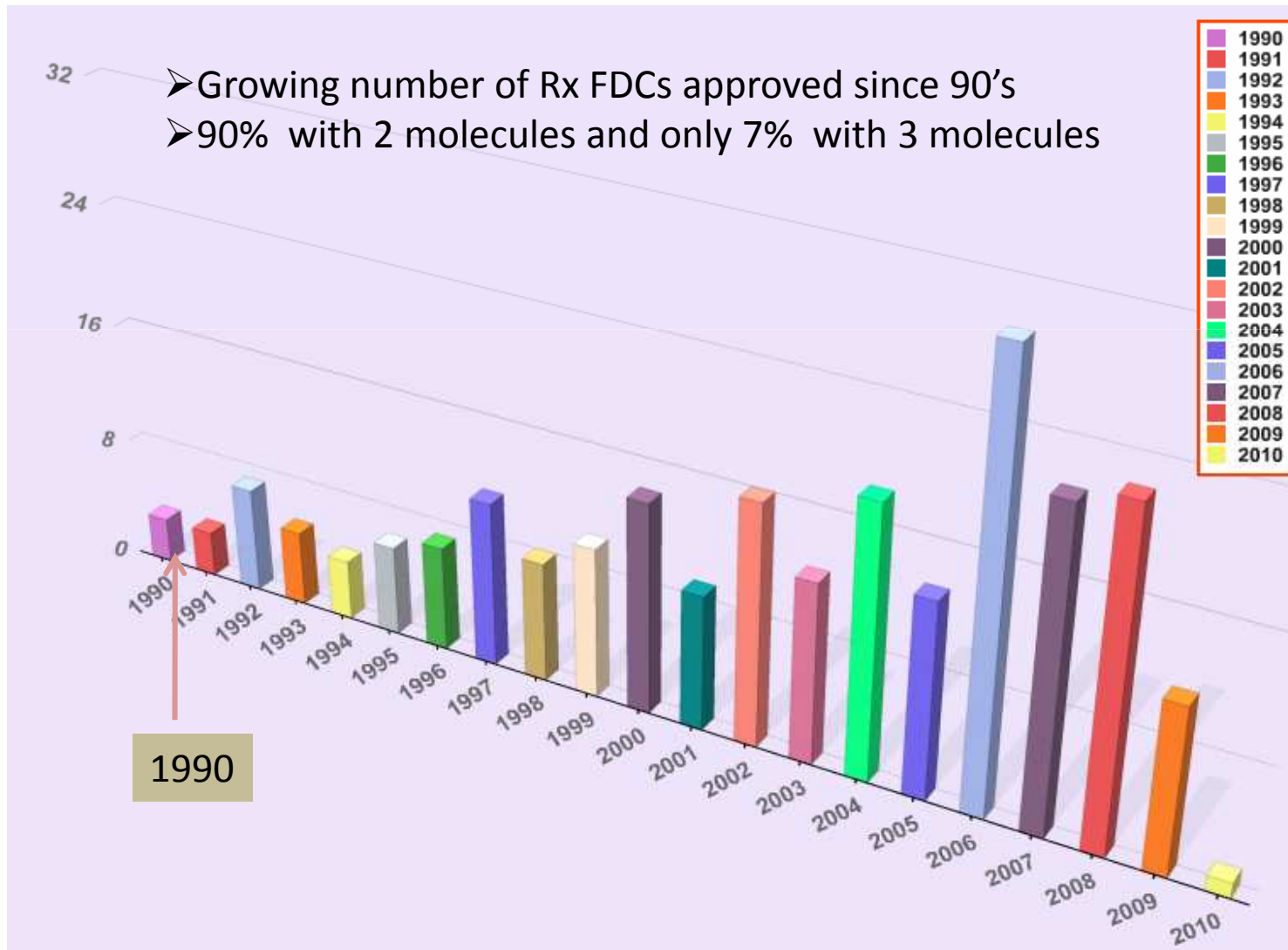
# MARKETED FDC PRODUCTS

n=1597



# MARKETED FDC PRODUCTS

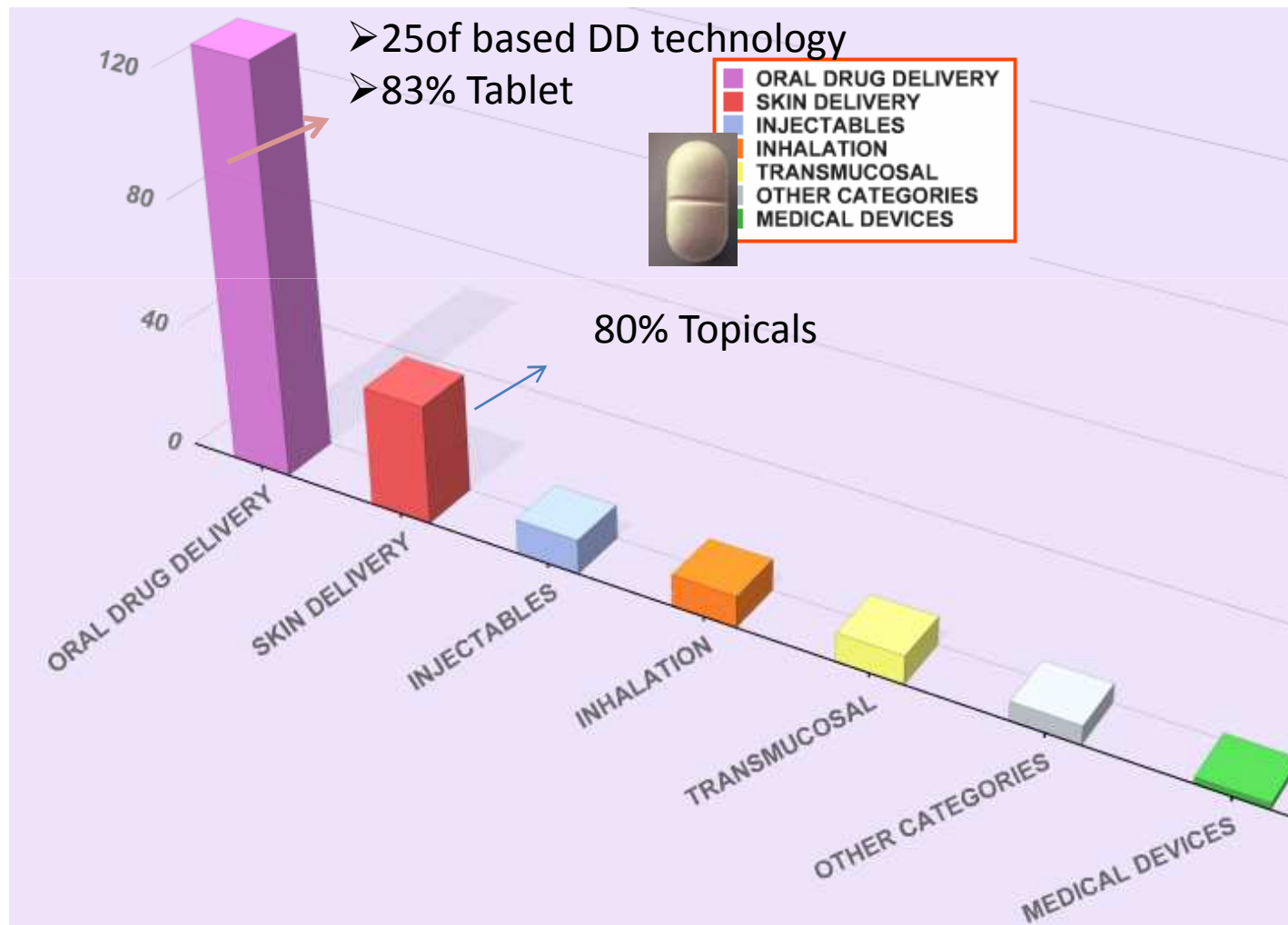
Includes, new combinations, indications and formulations and territories  
Exclude Generic/OTC and approvals, n=230



# ROUTES FOR MARKETED FDC PRODUCTS

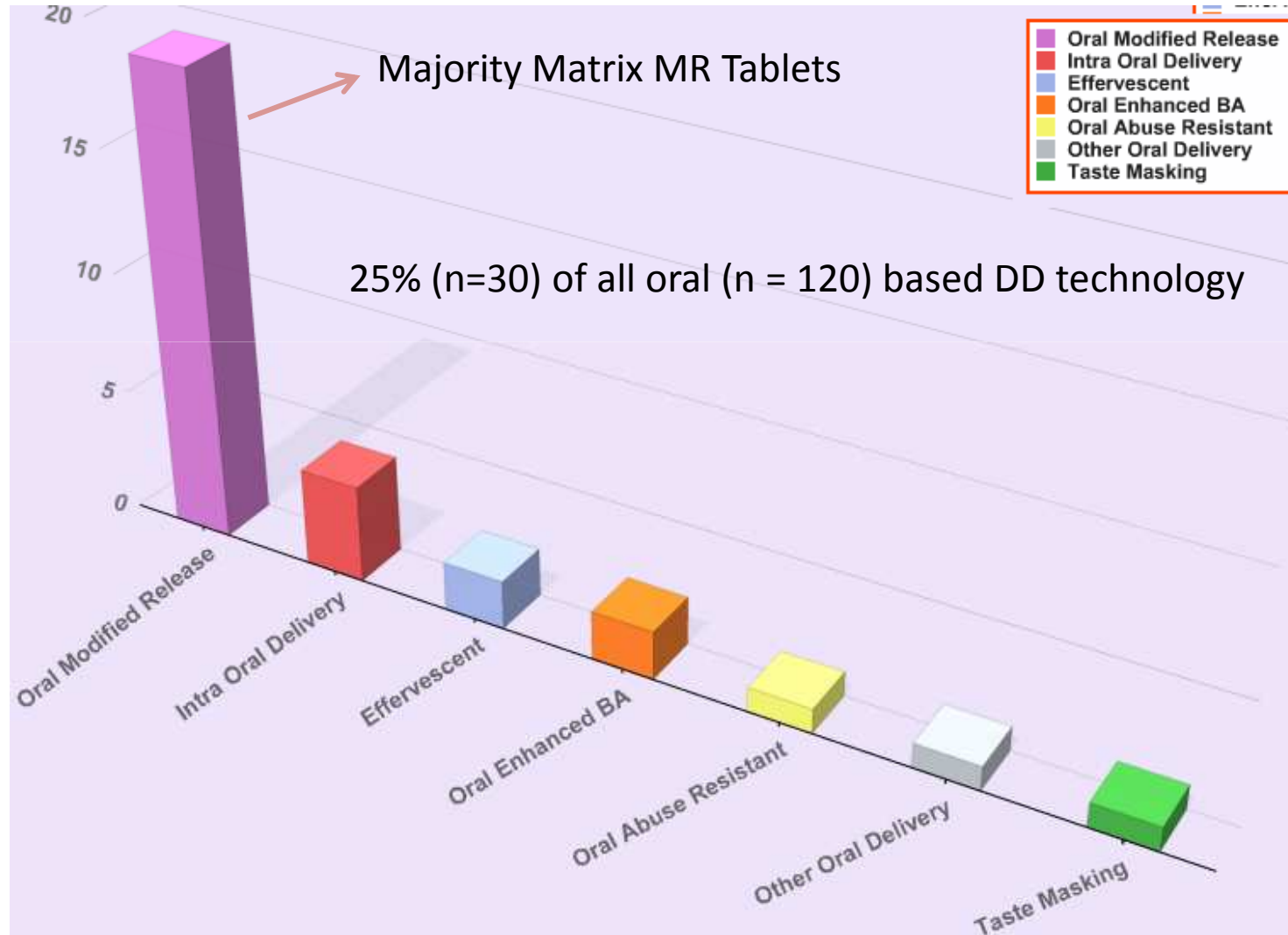
Includes, new combinations, indications and formulations and territories

Exclude Generic/OTC and approvals n=206



# MARKETED ORAL COMBO PRODUCTS

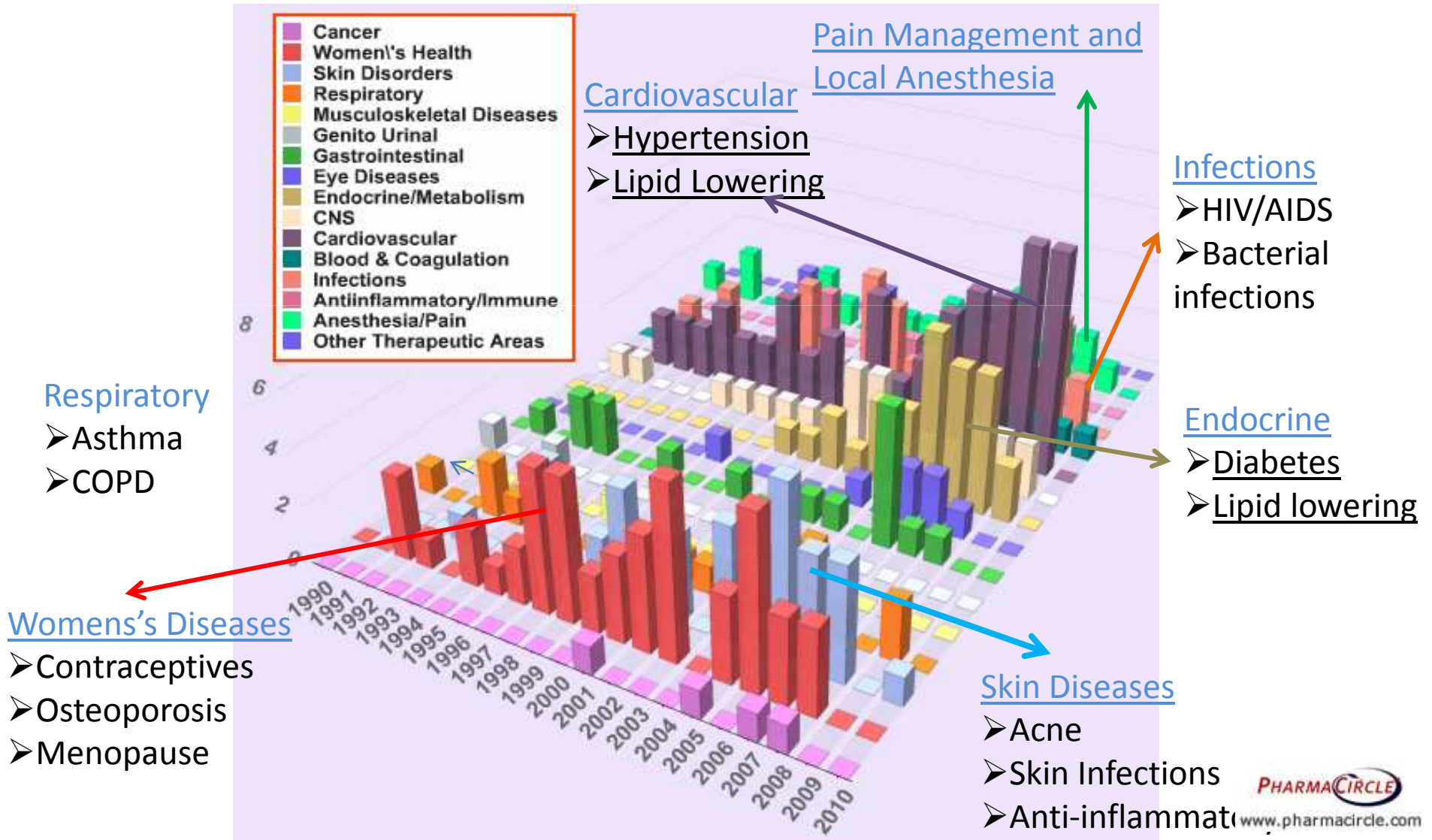
Includes, new combinations, indications and formulations and territories  
Exclude Generic/OTC and approvals , n=30



# APPROVALS VS. INDICATIONS (GLOBAL)

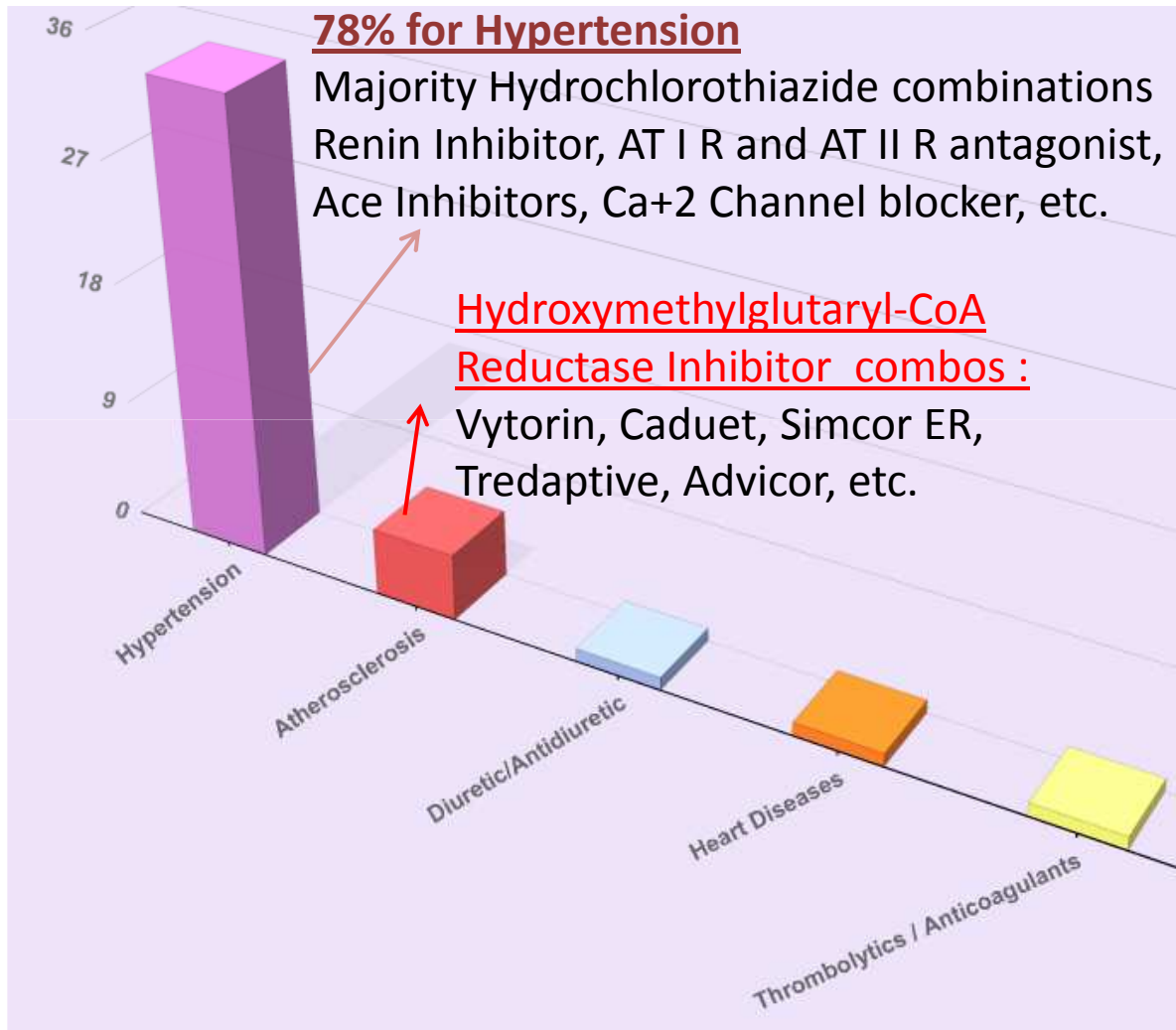
Includes, new combinations, indications and formulations and territories

Exclude Generic/OTC and approvals , n=234



# CARDIOVASCULAR FDCs

n=37

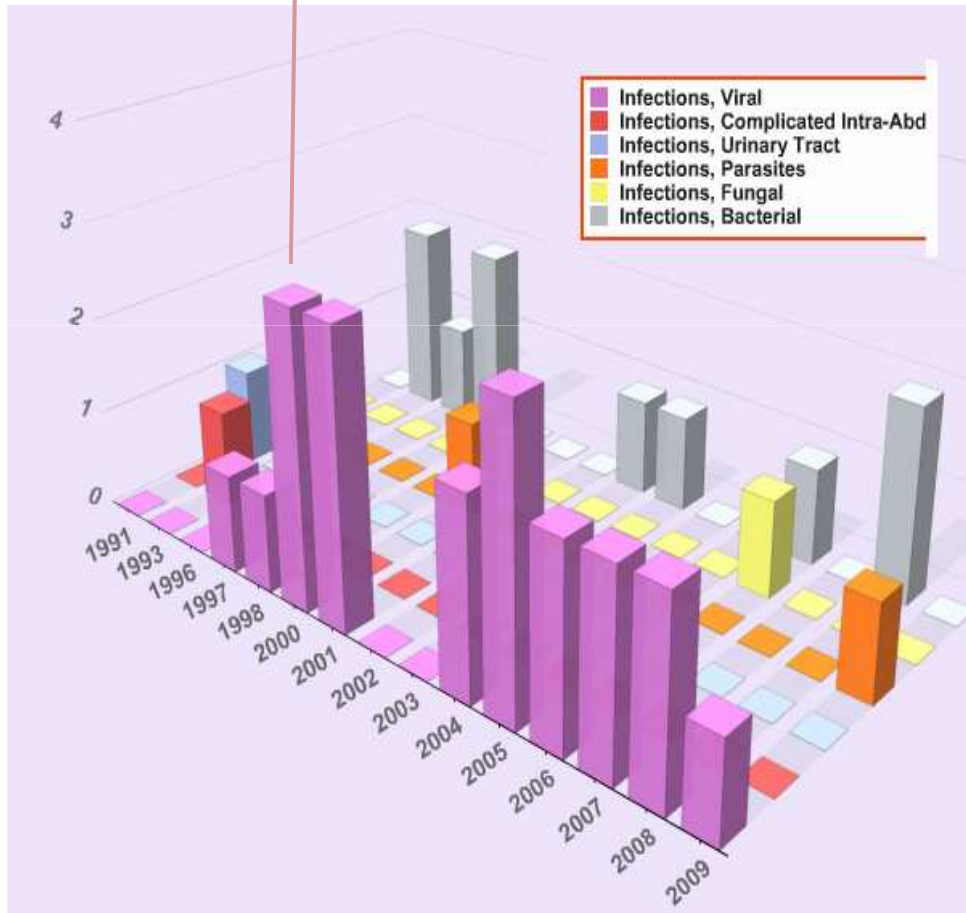


FDCs are likely to improve adherence in a range of settings, but uncertainty remains about the size of these benefits

# FDCs for INFECTION

n=35

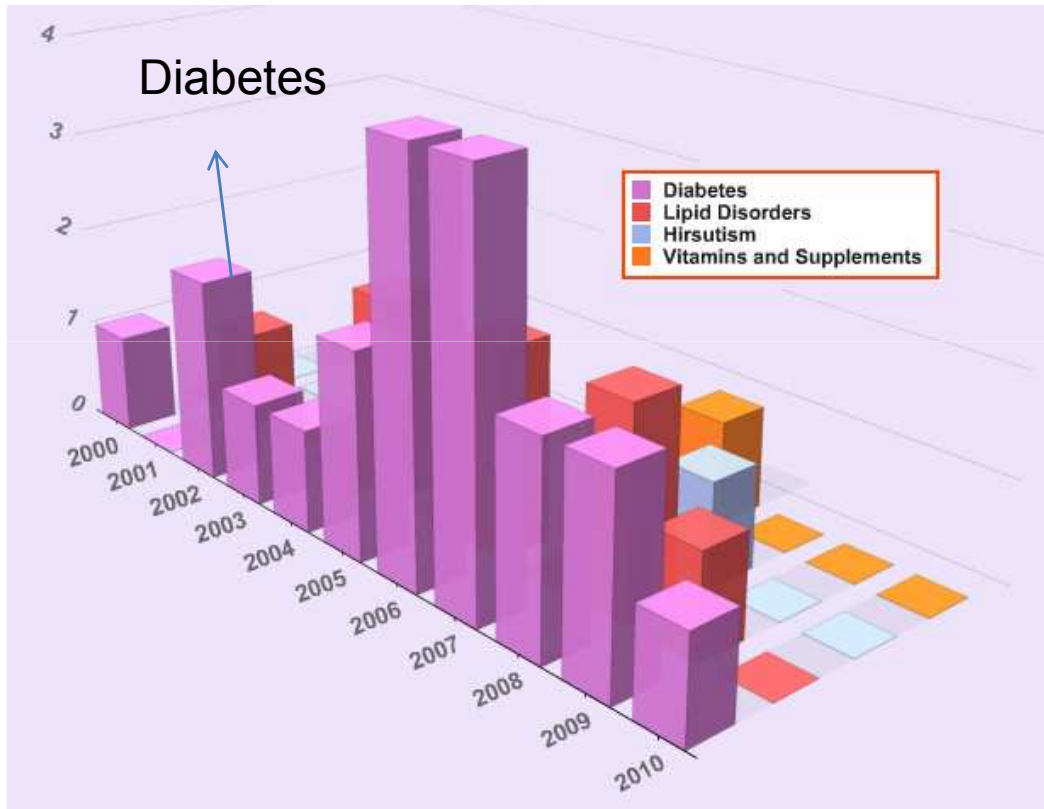
Viral Infections; HIV/AIDS, etc.



- Old gold standard for HIV: Combivir an FDC of zidovudine and lamivudine -2xday
- Newer FDCs with once daily dosing and improved tolerability and toxicity profiles
- Simplified dosing/handling-improved compliance, better disease control

# FDCs for ENDOCRINE/METABOLISM

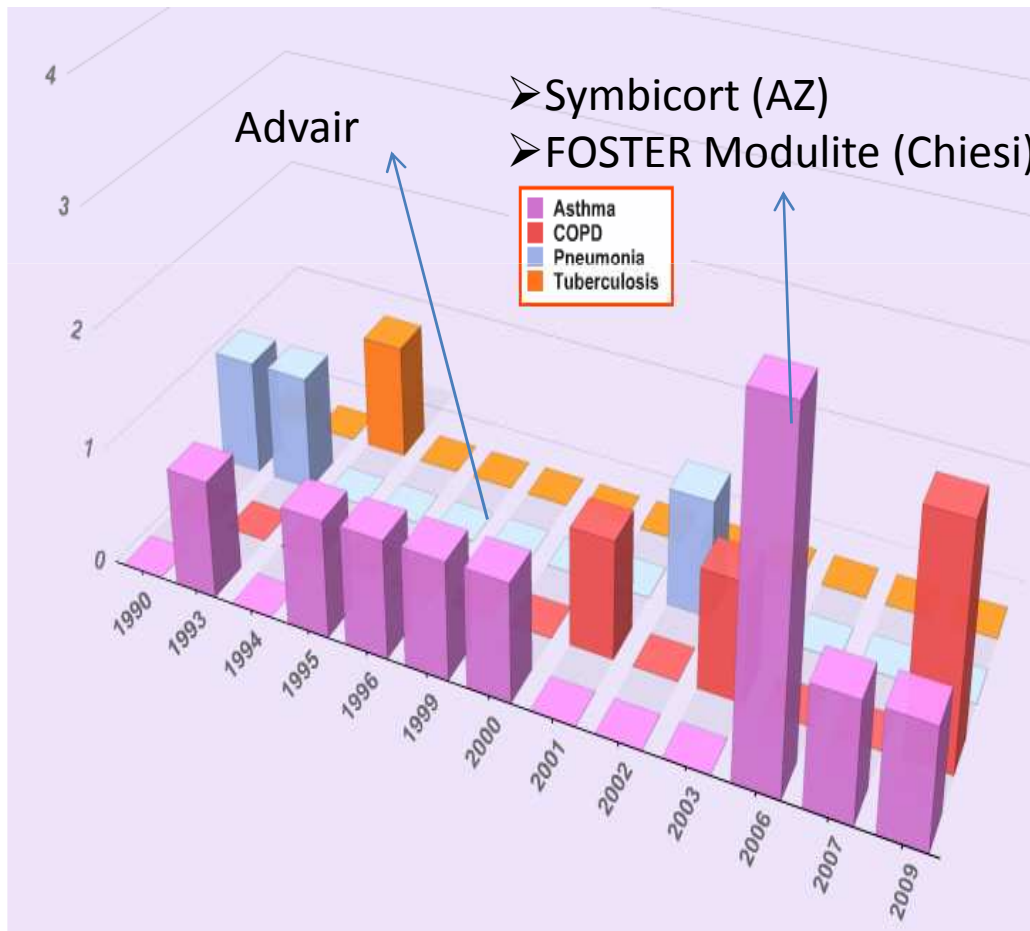
n=20



FDCs are likely to improve adherence in a range of settings, but uncertainty remains about the size of these benefits

# ASTHMA/COPD FDCs, n=30

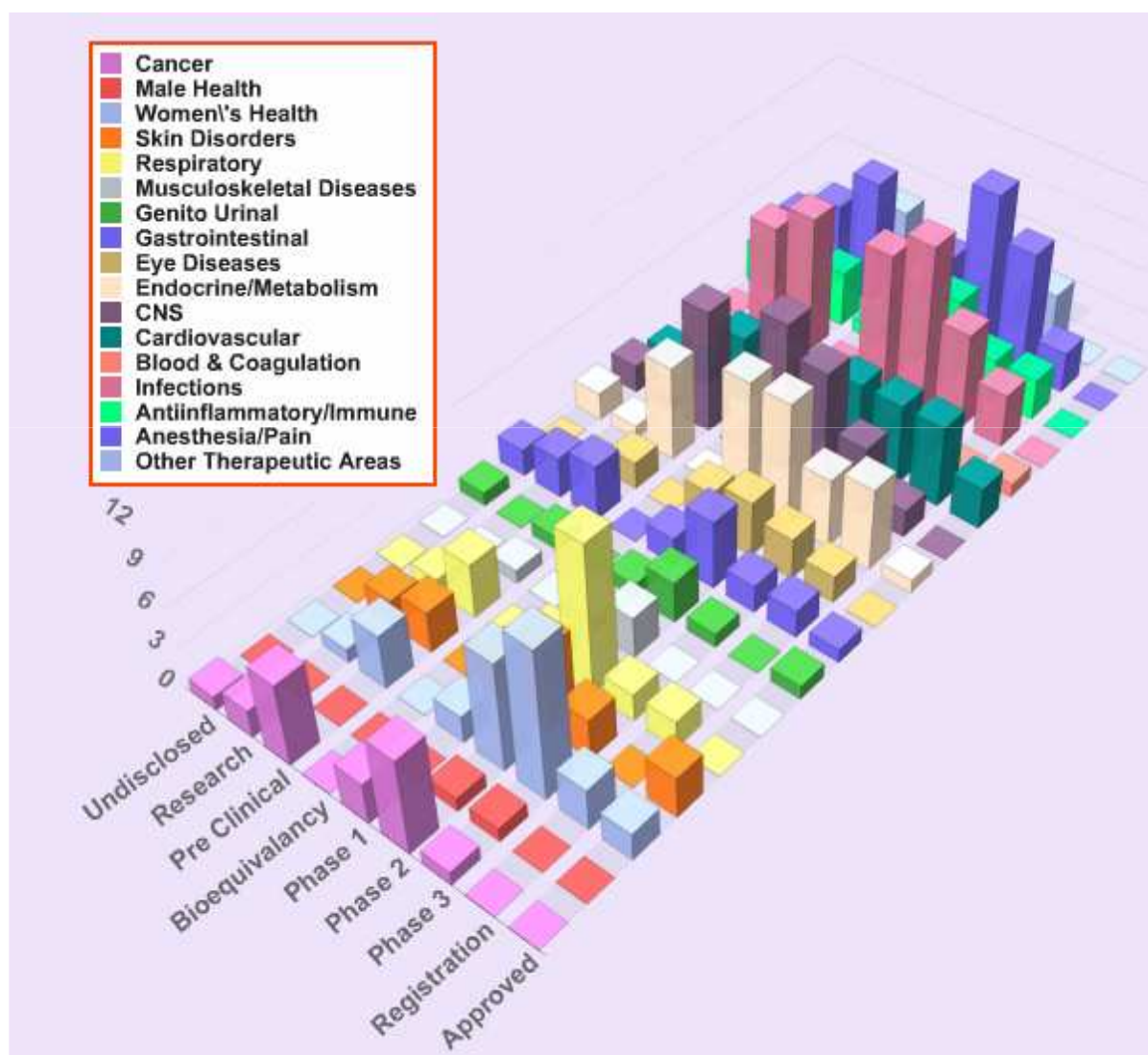
FDA recommends the use of FDCs containing an inhaled corticosteroid and a LABA because of the difficulty of ensuring compliance with both medications when they are administered separately



- Advair (GSK) and Symbicort (Astra Zeneca) combined sales \$9.5bil-50% of Inhalation market %18b-20 products

# FDC PIPELINE (GLOBAL)

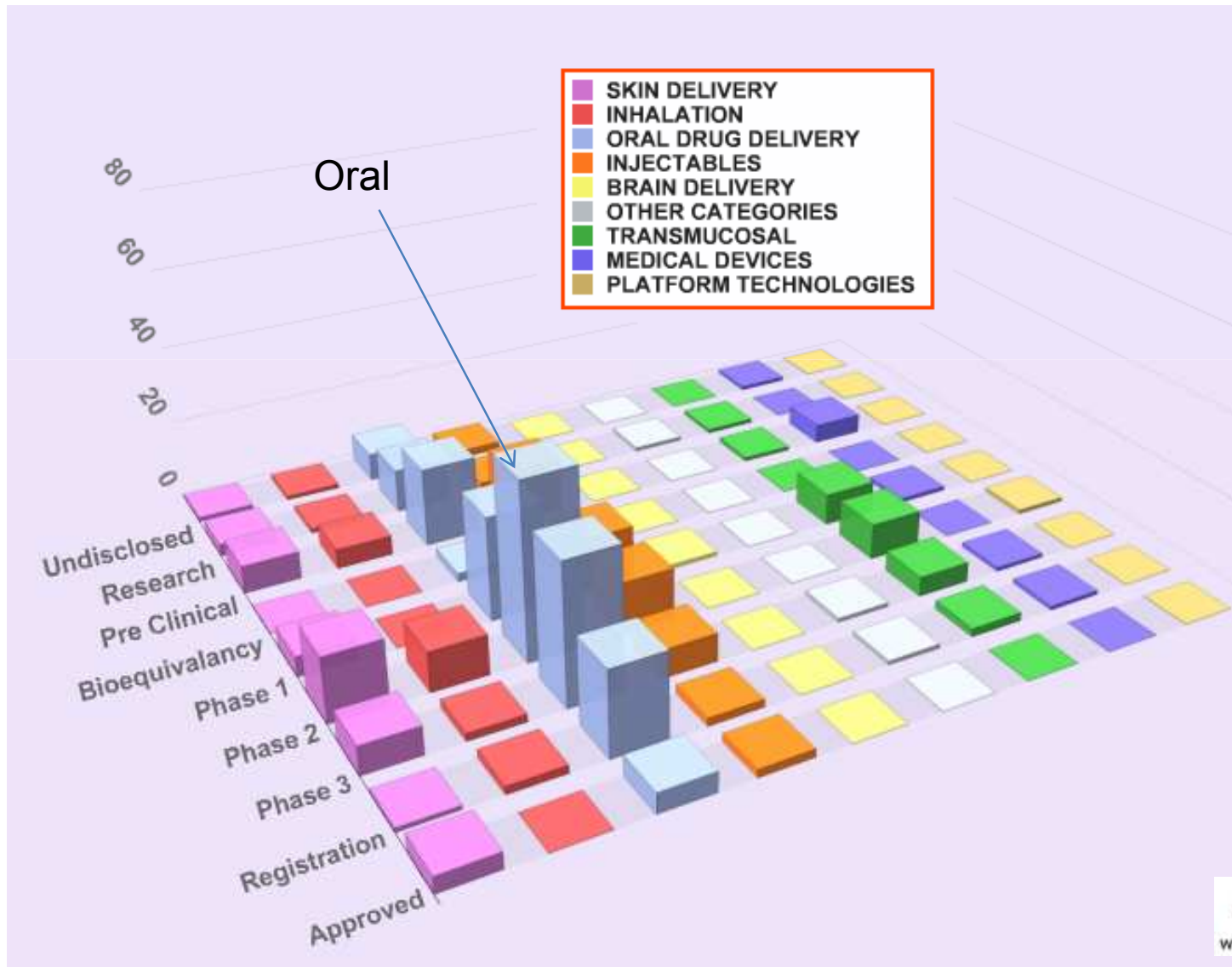
n=391



- Majority with 2 molecules
- Only 18 with have 3 mol. (HIV, Pain, Diabetes, etc.)
- 1 has 4 molecules (HIV)

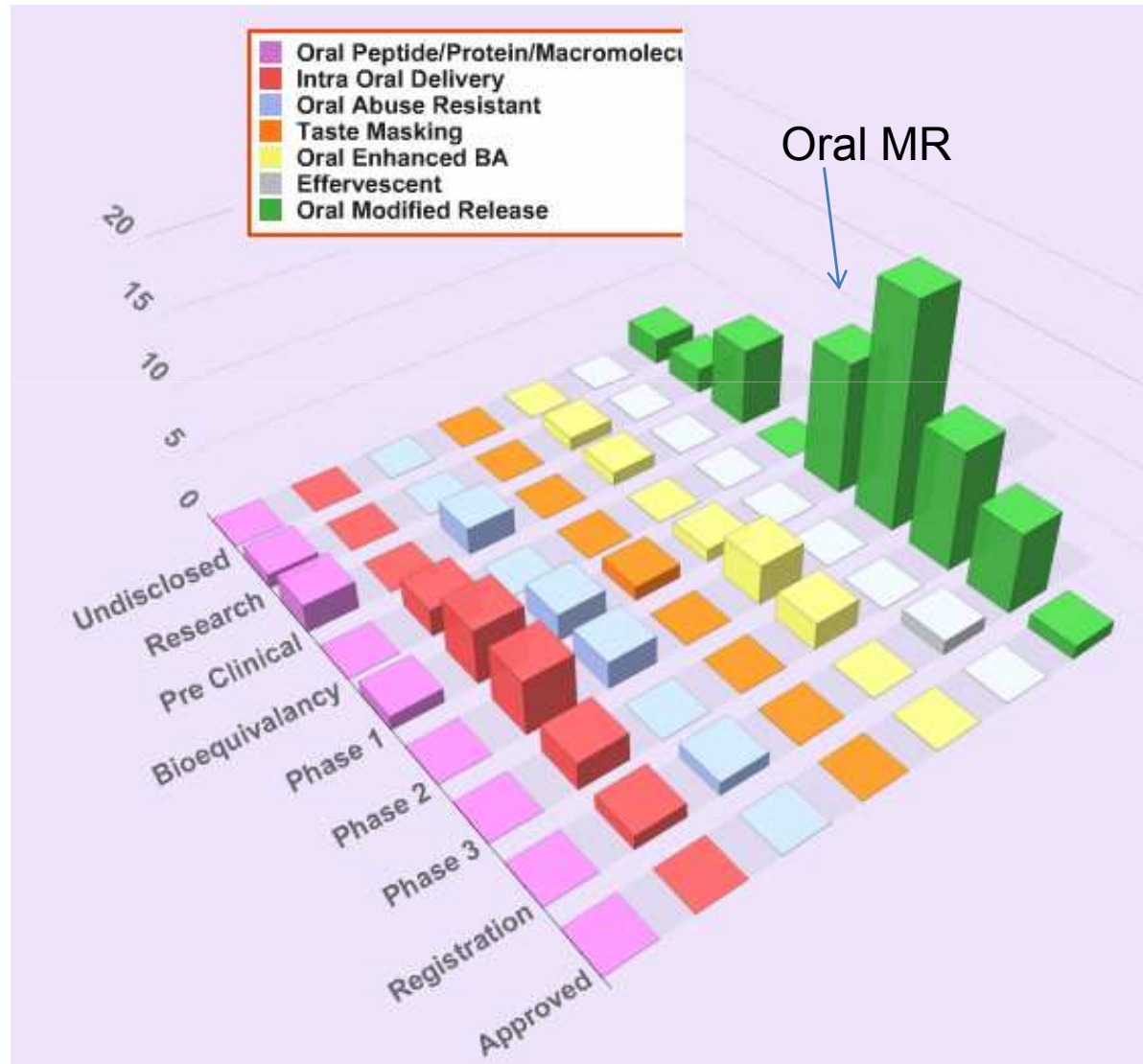
# ROUTES FOR FDC PIPELINE

n=332



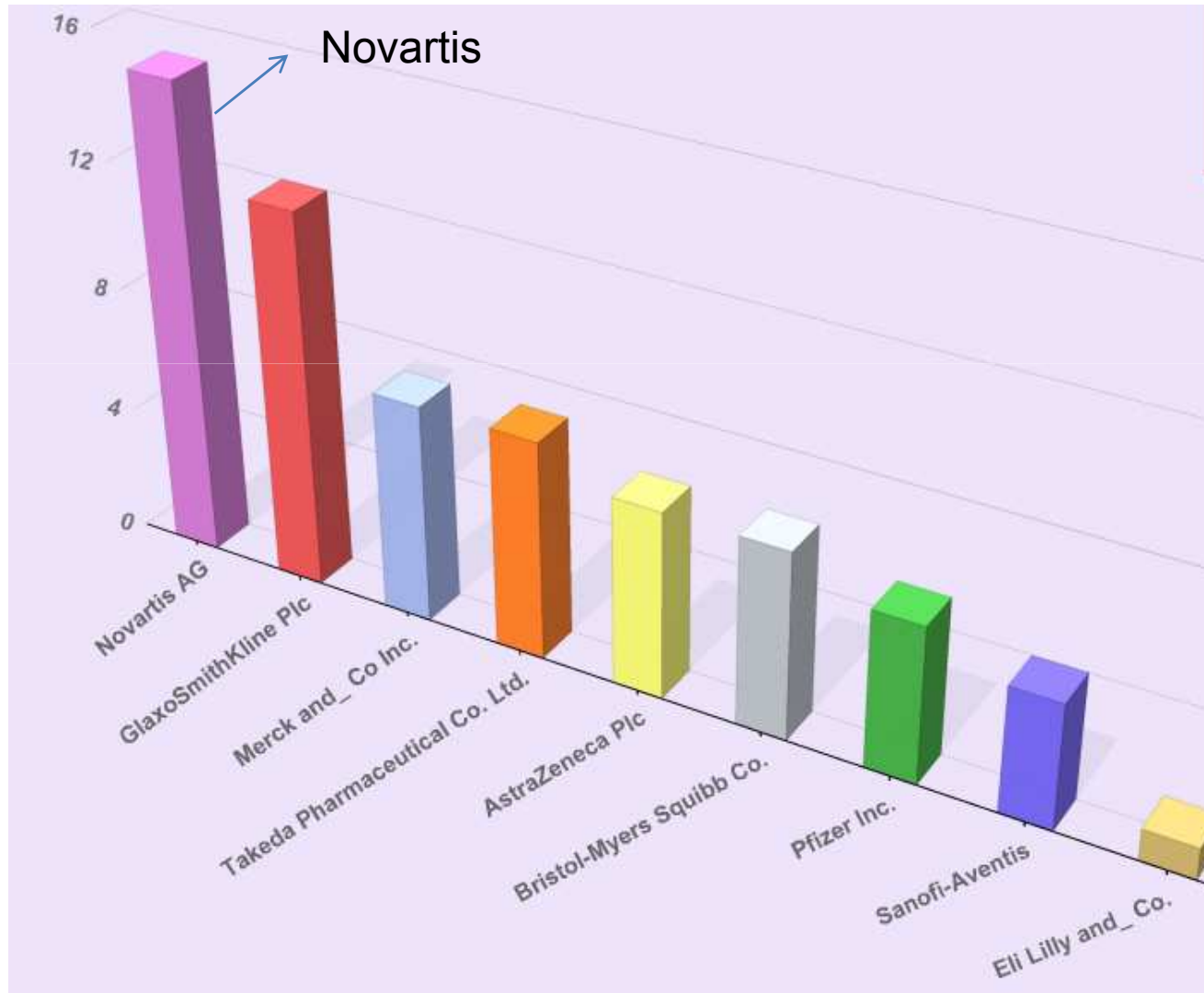
# ORAL FDC PIPELINE

n=87



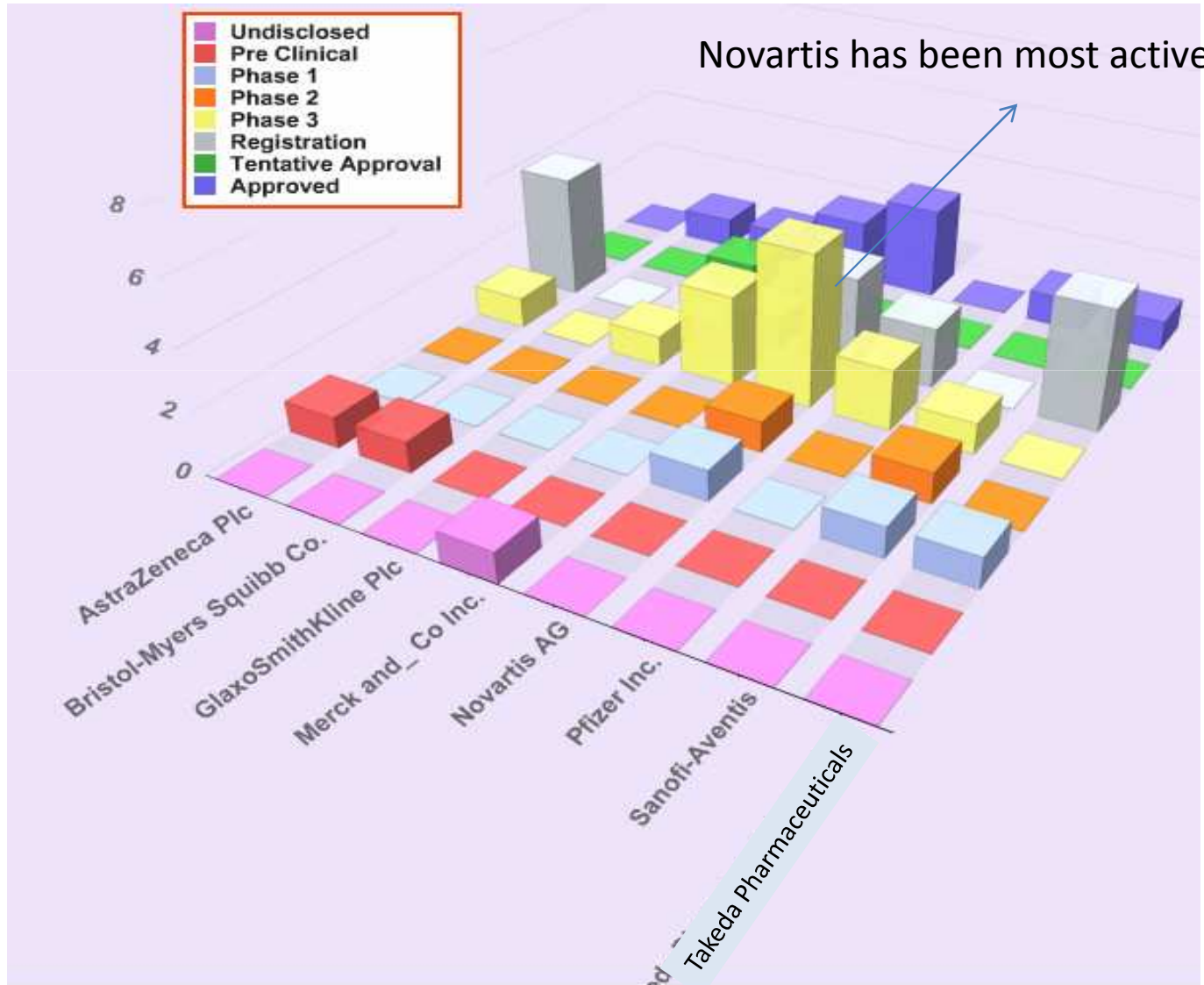
# FDCs MARKETED by LARGE PHARMA

Marketed since 1990 (no OTC), n=58



# FDC PIPELINE - LARGE PHARMA

n=45



# TOP SELLING FDC PRODUCTS

Name /Form	Molecules	Indication	Approval Year/ Company	Sales 2009 (\$Mil)
<b>Advair Discus/DPI/HFA</b>	fluticasone/salmeterol	Asthma/COPD	2000/GSK	7800
<b>Hyzaar/Cozaar</b>	losartan/HCT	Hypertension	1995/Merck & Co.	3561
<b>Truvada</b>	emtricitabine /tenofovir	HIV/AIDS	Gilead/2004	2490
<b>Atripla Tablets</b>	efavirenz/ emtricitabine/ tenofovir	HIV/AIDS	2007/Gilead/BMS	2382
<b>Vytorin</b>	ezetimibe /simvastatin	Lipid regulation	2004/Merck/SP	2352
<b>Symbicort /DPI/MDI</b>	budesonide/formoterol	Asthma/COPD	2006/Astra Zeneca	2004
<b>Avandamet Tablets</b>	rosiglitane/metformin	Diabetes	2002/GSK	1200
<b>Kaletra soft gel</b>	lopinavir /ritonavir	HIV/AIDS	2000/Abbott	1366
<b>Epzicom</b>	abacavir /lamivudine	HIV/AIDS	2005/Shire	854
<b>Combivir Tablets</b>	lamivudine /zidovudine	HIV/AIDS	1997/Shire	665

# RECENT FDC APPROVALS

Product	Molecules	Indications	Approval/Company
Ristfor Tablet	sitagliptin/metformin	Diabetes	March 10/Merck(EU)
Duodart	dutasteride/tamsulosin	BPH	March 10/GSK (EU) Tent. Approved Jan. 10 (USA)
DuoCover/DuoPlavin tablet	clopidogre/aspirin	ACS/MI	March 2010 BMS/SA (EU)
Azor Tablet	amlodipine /olmesartan	Hypertension	08/09/Daiichi Sankyo (USA&EU)
EMBEDA Abuse resistant capsule	morphine /naltrexone	Pain	09/Alpharma/King Pharma (USA)
Lipsovir cream	acyclovir /hydrocortisone	Herpes	09/Medivir/Meda (USA)
Copalia HCT	amlodipine /valsartan/ hydrochlorothiazide	Hypertension	09/Novartis (EU)
ACTOplus met XR Tablets	metformin/pioglitazone	Diabetes	09/Takeda (USA)

# CONCLUSIONS

- FDCs may offer better treatment through improving patient compliance
- Greater the noncompliance chance with individual drugs higher the chance of FDC product success
- New products with patent/market exclusivity. Overcome formulation challenges for stronger patents
- Growing number of products/pipeline for cardiovascular, lipid regulation, diabetes, pain, respiratory diseases and infections
- Majority are based on two molecules, and several 3 mol. FDCs for HIV, Diabetes, Hypertension, etc. and even 4 mol FDCs for HIV
- Majority are delivered as IR/MR tablets. Also Inhalation, Topical and Transdermal products

# QUESTIONS?

Tugrul Kararli, Ph.D. MBA  
Pharmacircle

[www.pharmacircle.com](http://www.pharmacircle.com)  
[tkararli@pharmacircle.com](mailto:tkararli@pharmacircle.com)

(760) 436 1199