

## **Brian Daniels, M.D.**

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Global Development & Medical Affairs

# Oncology

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# Metastatic Melanoma Unmet Need

- ◆ **140,000 cases of metastatic melanoma worldwide leading to 40,000 deaths annually**
- ◆ **Half of patients are age 59 or younger**
- ◆ **Global standard of care, dacarbazine (DTIC), provides 6-9 months median survival in first-line**
- ◆ **Clinical guidelines recommend investigational agents**

# Ipilimumab: Potential Product Profile of a Novel Immunotherapy

Mechanism of Action	Efficacy	Safety	Dosing
<ul style="list-style-type: none"> <li>◆ Monoclonal antibody that selectively blocks CTLA-4 and enhances antitumor responses</li> <li>◆ Reactivates patient's own immune system</li> <li>◆ Unique response patterns</li> </ul>	<ul style="list-style-type: none"> <li>◆ Durable response after immune system is reactivated</li> <li>◆ Improved survival</li> <li>◆ Evidence for efficacy in several types of malignancies</li> </ul>	<ul style="list-style-type: none"> <li>◆ Mechanism-based, immune-related adverse events</li> <li>◆ Well-established recommendations for managing adverse events</li> </ul>	<ul style="list-style-type: none"> <li>◆ Initial dosing: One infusion every three weeks</li> <li>◆ Maintenance dosing: One infusion every three months</li> </ul>

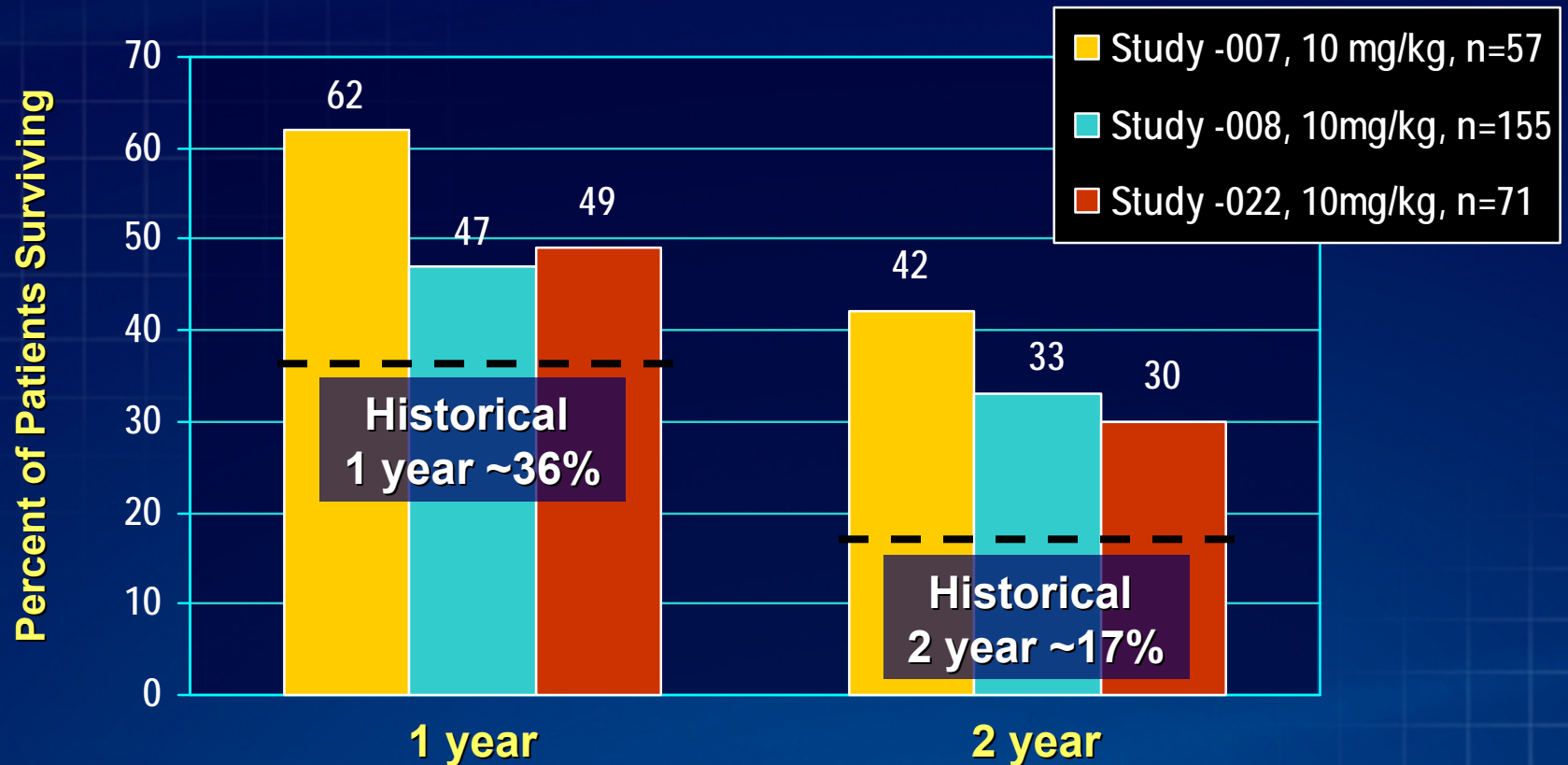
# **Ipilimumab: Novel Immunotherapy with a Unique Tumor Response Pattern**

- ◆ **By selectively inhibiting CTLA-4, ipilimumab removes one potential “brake” on a patient’s immune system**
- ◆ **Leads to reactivation of the immune system which can then target the tumor**
- ◆ **Clinical responses occur over a broad range of time and unique response patterns have been identified**
- ◆ **Potential for durable effect and prolongation of survival in patients with a variety of response patterns**

# Ipilimumab: Registrational Program for Monotherapy and Combination Therapy in Advanced Melanoma

Patient Type	Study #	Key Features
Pretreated	-008 (N=155)	◆ Rapid progression after prior therapy
	-022 (N=217)	◆ Dose ranging in patients with progression or intolerance to prior therapy
	-007 (N=115)	◆ Investigate prophylactic budesonide to prevent GI adverse events
	-020 (N=676)	◆ Ipilimumab combination with gp100 vaccine vs. ipilimumab alone vs. gp100 vaccine alone
Naïve	-024 (N=502)	◆ Ipilimumab combination with DTIC vs. DTIC alone; First-line survival study
Adjuvant	-029 (N=950)	◆ Ipilimumab vs. placebo after complete resection of stage 3 melanoma

# Ipilimumab: Encouraging Overall Survival at One and Two Years in 2<sup>nd</sup>-line Metastatic Melanoma



Ipilimumab data at 10mg/kg from Phase II studies -007, -008, -022, O'Day et al. ASCO, June 2009

Historical data: Korn et al., J. Clin. Oncol. 2008; Meta analysis of 42 Phase 2 trials

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# Ipilimumab: Additional Clinical Profile

- ◆ Efficacy observed in melanoma patients with brain metastases
- ◆ Potential to personalize therapy
- ◆ At 10 mg/kg an average of 25% of patients experience grade 3 or 4 immune-related adverse events

# Ipilimumab: Value in Melanoma

<b>Challenges</b>	<ul style="list-style-type: none"><li>◆ Unique response kinetics and patterns</li><li>◆ Management of immune-related adverse events</li></ul>
<b>Differentiation</b>	<ul style="list-style-type: none"><li>◆ Novel immunotherapy working through patient's immune system with potential for activity in several tumors</li></ul>
<b>Patient Outcomes</b>	<ul style="list-style-type: none"><li>◆ Potential for durable clinical responses leading to improved long-term survival</li></ul>
<b>Economic Value</b>	<ul style="list-style-type: none"><li>◆ In melanoma, potential for meaningful durable remissions in young, working age patients</li></ul>

# Ipilimumab: Program and Data Flow

<b>Tumor type</b>	<b>Study</b>	<b>Data Flow</b>
<b>Metastatic melanoma</b>	<b>-020</b> <b>-024</b>	<b>Potential US and EU submissions in 2010</b> <ul style="list-style-type: none"> <li>◆ <b>Vaccine combination/monotherapy study: submitted for presentation at ASCO 2010</b></li> <li>◆ <b>Treatment-naïve, event driven study in combination with DTIC: Results expected 2010</b></li> </ul>
<b>Lung cancer (Ph II)</b>	<b>-041</b>	<b>NSCLC &amp; SCLC</b> <ul style="list-style-type: none"> <li>◆ <b>Immune-related progression-free survival: 2010 (NSCLC submitted for presentation at ASCO 2010)</b></li> <li>◆ <b>Overall survival: 2011</b></li> </ul>
<b>Melanoma brain metastases (Ph II)</b>	<b>-042</b>	<ul style="list-style-type: none"> <li>◆ <b>Response and duration data: submitted for presentation at ASCO 2010</b></li> <li>◆ <b>Overall survival data: 2011</b></li> </ul>
<b>Prostate cancer (Ph III)</b>	<b>-043</b>	<ul style="list-style-type: none"> <li>◆ <b>Phase III ongoing</b></li> </ul>

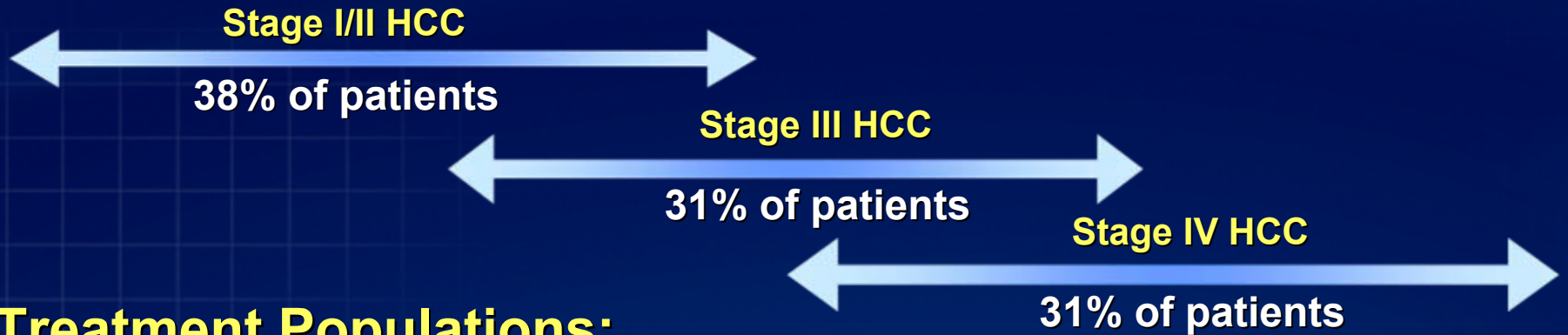
# Hepatocellular Carcinoma (HCC) is a Global Disease with Significant Unmet Medical Need

- ◆ **BMS is committed to liver diseases through Baraclude (hepatitis B), belatacept (liver transplant), brivanib (hepatocellular carcinoma) and innovative medicines for hepatitis C**
- ◆ **700,000 new patients are diagnosed with HCC each year**
- ◆ **Fourth leading cause of cancer death worldwide**
- ◆ **One approved therapy for patients who cannot be cured with surgery**
- ◆ **High disease burden in emerging markets and Asia Pacific**

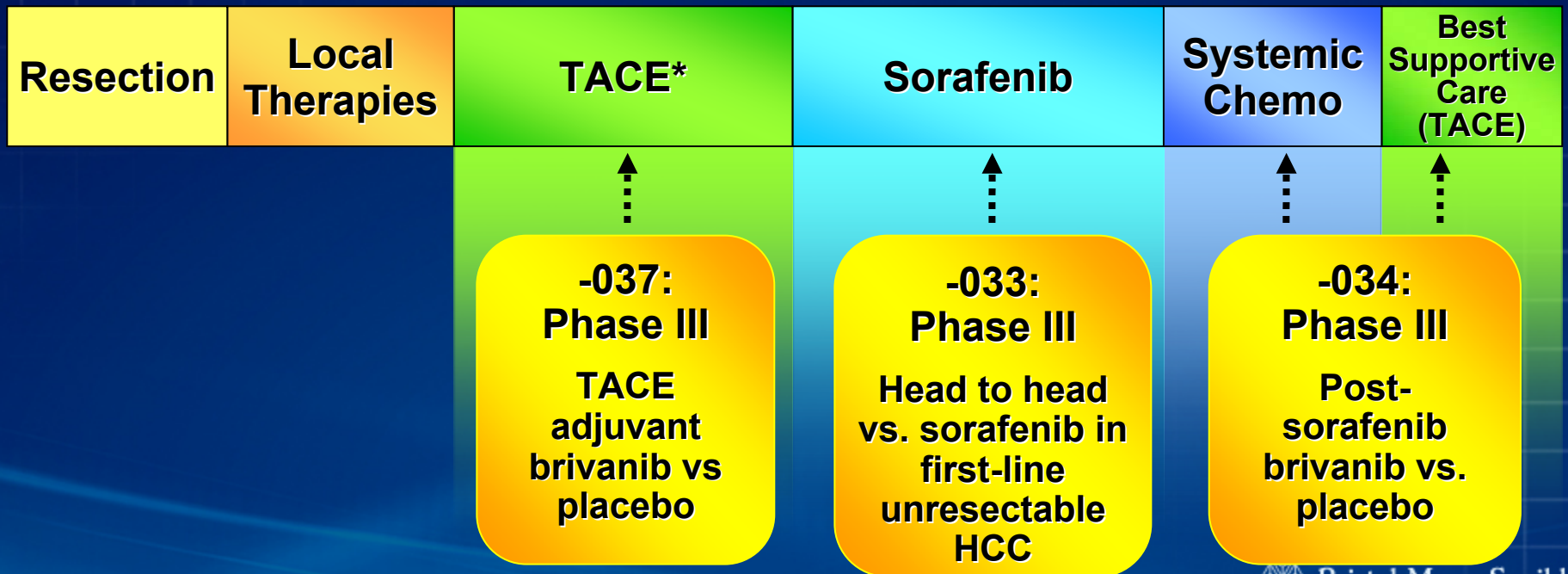
# Brivanib: Novel Opportunity for Broad Cancer Treatment Beyond VEGF Inhibition

Mechanism of Action	Efficacy	Safety	Dosing
<ul style="list-style-type: none"> <li>◆ Dual selective inhibitor of FGF and VEGF pathways</li> <li>◆ FGF over-expression indicated in tumor escape from VEGF inhibitors</li> <li>◆ FGF over-expression prognostic for poor outcomes</li> </ul>	<ul style="list-style-type: none"> <li>◆ Potential for superior efficacy to current VEGF inhibitors</li> <li>◆ Effective after progress on sorafenib</li> <li>◆ Exploring personalized medicine approach</li> <li>◆ Early efficacy signal in CRC and breast cancer</li> </ul>	<ul style="list-style-type: none"> <li>◆ Manageable safety profile</li> <li>◆ Most frequent adverse events: fatigue, hypertension, and GI symptoms</li> </ul>	<ul style="list-style-type: none"> <li>◆ Oral, once daily therapy</li> </ul>

# Brivanib: HCC Registrational Program



## Treatment Populations:



\*TACE: Transarterial chemoembolization

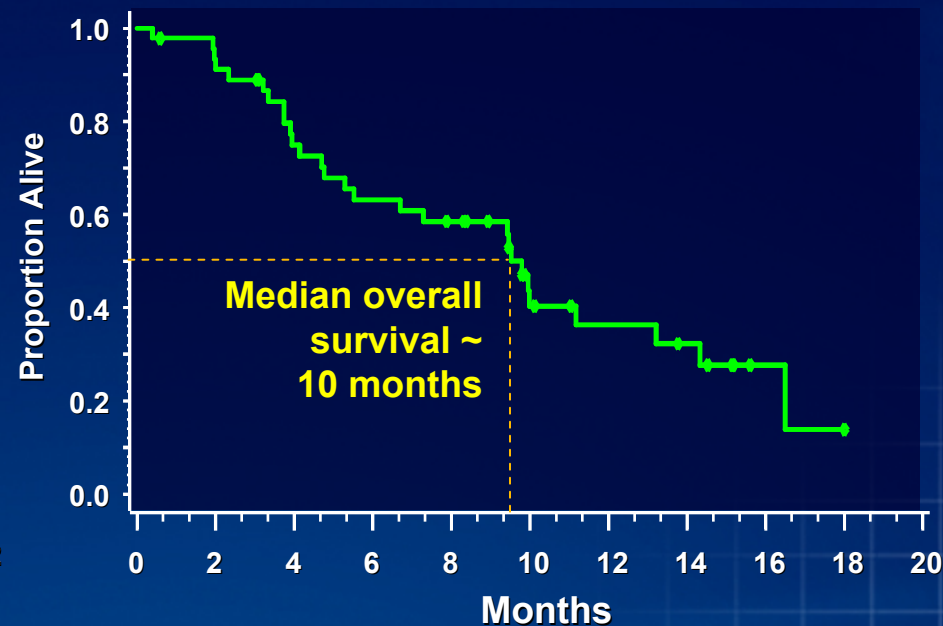
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# Brivanib: Results from a Phase II Study in HCC Demonstrated Encouraging Clinical Activity

## First-line Treatment n = 55



## Second-line Treatment n = 46



### Historical Comparison

Majority of patients were from Asia where current standard of care provides overall survival of 6.5 months in first-line

# Brivanib: Additional Clinical Profile

- ◆ **Most HCC patients with elevated alpha-fetoprotein show significant decreases with therapy**
- ◆ **Efficacy in late line CRC in combination with Erbitux**
- ◆ **Activity seen in sarcoma and other tumors in Phase II with potential for a personalized medicine approach**
- ◆ **Manageable safety profile**
  - **Most adverse events were mild (grade 1 and 2)**
  - **Adverse events were similar to other medicines in this class (fatigue, hypertension and GI)**
  - **Limited hematologic and dermatologic toxicities**

# Brivanib: Value in HCC

<b>Challenges</b>	<ul style="list-style-type: none"><li>◆ Emerging market disease prevalence</li><li>◆ Head-to-head comparison with standard of care</li></ul>
<b>Differentiation</b>	<ul style="list-style-type: none"><li>◆ Selectively inhibits two important pathways in tumor biology, VEGF and FGF with potential advantage over other VEGF inhibitors</li></ul>
<b>Patient Outcomes</b>	<ul style="list-style-type: none"><li>◆ Potential to improve survival in a range of HCC patients as well as other tumors</li></ul>
<b>Economic Value</b>	<ul style="list-style-type: none"><li>◆ In first line HCC directly comparing to sorafenib to demonstrate relative value of brivanib</li></ul>

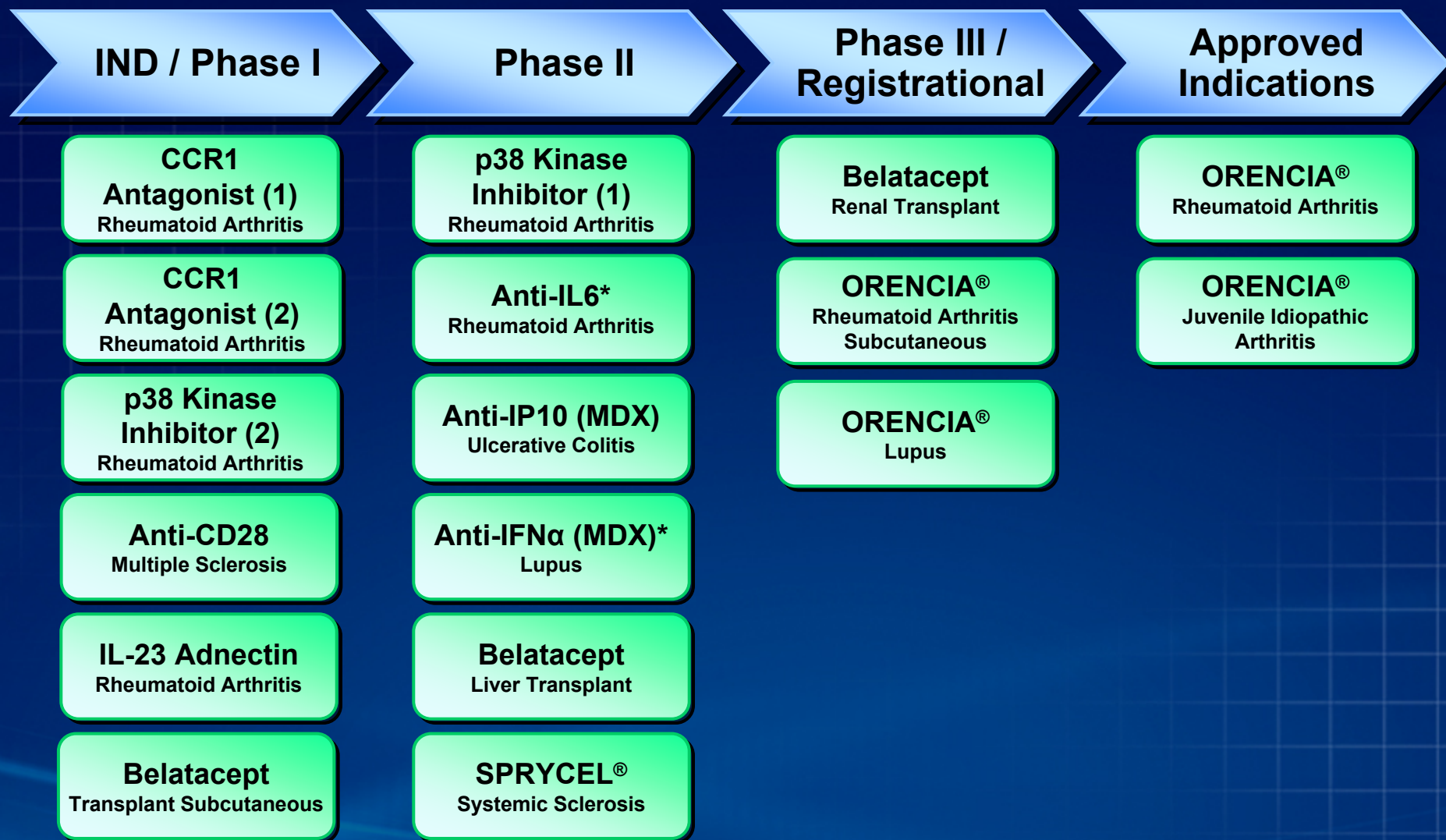
# Brivanib: Program and Data Flow

<b>Tumor type</b>	<b>Study</b>	<b>Data Flow</b>
<b>Hepatocellular carcinoma (HCC)</b>	<b>Ph II open label study</b>	◆ <b>New response criteria: ASCO GI, January 2010</b>
	<b>Ph III -034, post-sorafenib</b>	◆ <b>Data available 2011 (event-driven)</b> ◆ <b>US and EU submission targeted 2011</b>
	<b>Ph III -033, first-line</b>	◆ <b>Data available 2012</b>
	<b>Ph III -037, TACE adjuvant</b>	
<b>Colorectal cancer</b>	<b>Ph I / II -025, second-line combination with irinotecan and Erbitux</b>	◆ <b>Data available 2011</b>
	<b>Ph III -009, third-line combination with Erbitux</b>	
<b>Sarcoma</b>	<b>Ph II -026</b>	

# Immunoscience

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# Immunoscience – Development Portfolio



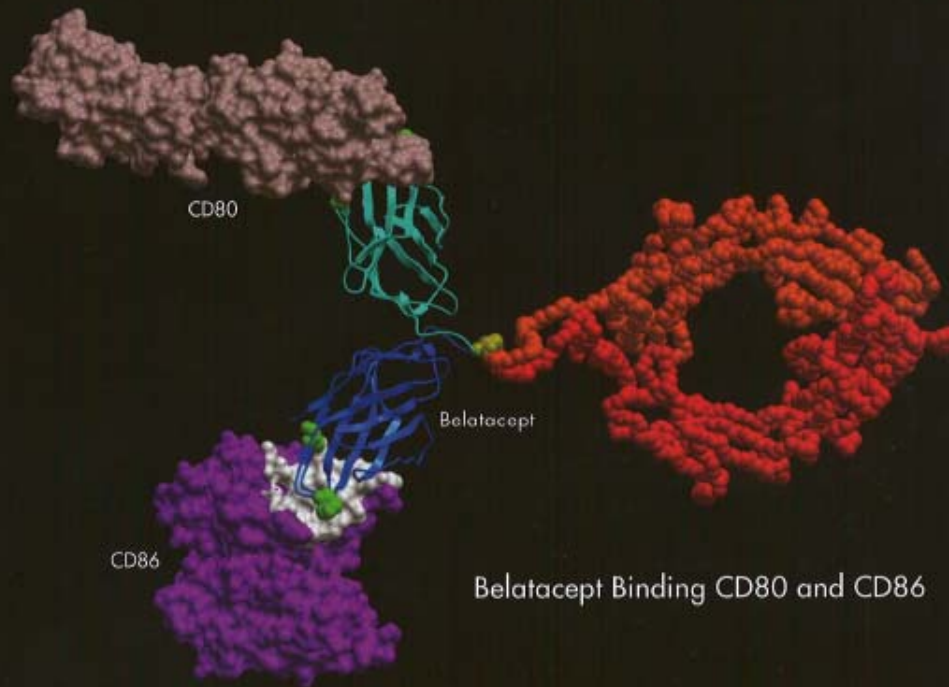
\* In Partnership Anti-IL6: Alder BioPharmaceuticals; Anti-IFN $\alpha$ : MedImmune/AstraZeneca

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# American Journal of Transplantation



THE OFFICIAL JOURNAL OF THE AMERICAN SOCIETY OF TRANSPLANTATION  
AND THE AMERICAN SOCIETY OF TRANSPLANT SURGEONS



WILEY-BLACKWELL

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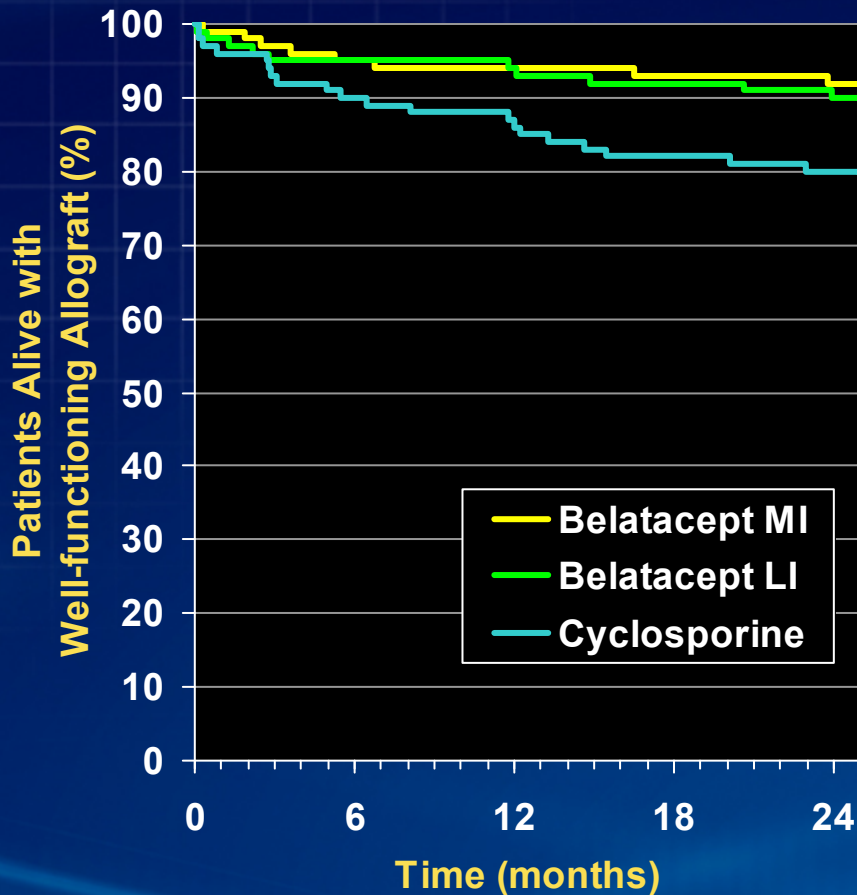
Bristol-Myers Squibb

# Significant Need to Improve Long-Term Outcomes in Kidney Transplant

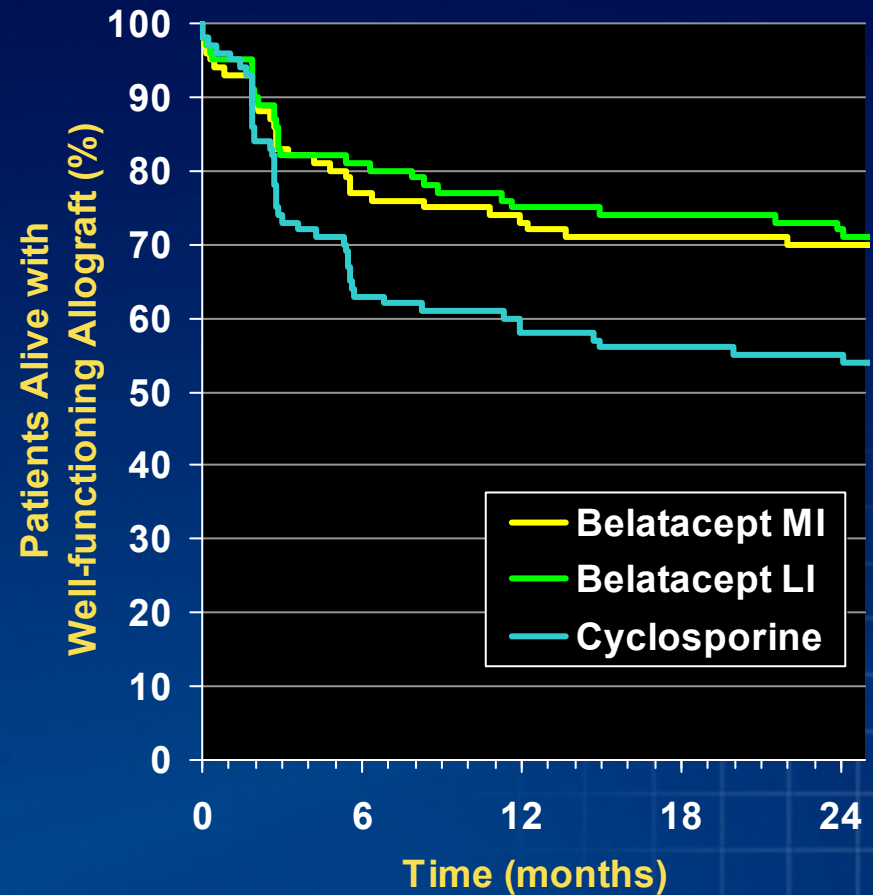
- ◆ **Long-term patient and graft survival**
  - One year survival rates >90%
  - Five year survival rates 66% – 79%
- ◆ **Chronic allograft nephropathy (CAN) and cardiovascular disease are the most frequent causes of graft loss and death**
- ◆ **Calcineurin Inhibitors (CNIs) are associated with complications including nephrotoxicity, hypertension, diabetes and hyperlipidemia**

# Belatacept: Impact on Renal Function and Patient and Graft Survival

## Standard Criteria Donor



## Extended Criteria Donor



MI = More Intensive, LI = Less Intensive dose regimen

Time to first of two GFR measures <30, death or graft loss

Ph III Study -008 and -027, 2-year data, targeted for presentation at ATC, May 2010

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# Belatacept: Potential Alternative to Current Standard of Care in Transplantation

Mechanism of Action	Efficacy	Safety	Dosing
<ul style="list-style-type: none"> <li>◆ Selective co-stimulation blocker of T-cells that leads to a targeted immunosuppressive effect</li> </ul>	<ul style="list-style-type: none"> <li>◆ High rates of early patient and graft survival</li> <li>◆ Potential for improved long-term patient and graft survival</li> <li>◆ Healthier kidneys: Superior renal function and less CAN</li> <li>◆ Efficacy in a broad range of transplant kidneys and patients</li> <li>◆ Higher acute rejection rates in one study</li> </ul>	<ul style="list-style-type: none"> <li>◆ Similar rates of infections                             <ul style="list-style-type: none"> <li>- One PML case in renal program</li> </ul> </li> <li>◆ Improved cardiovascular and metabolic risk profile</li> <li>◆ Increase in PTLD</li> <li>◆ Risk evaluation and mitigation strategy (REMS) proposed</li> </ul>	<ul style="list-style-type: none"> <li>◆ Intravenous formulation</li> <li>◆ Recommend less intense regimen for use</li> </ul>

# Belatacept: Value in Renal Transplantation

<b>Challenges</b>	<ul style="list-style-type: none"><li>◆ Paradigm shift to focus on long-term outcomes</li><li>◆ Market uptake, as indication will be for new transplants and will require IV infusion</li></ul>
<b>Differentiation</b>	<ul style="list-style-type: none"><li>◆ Improvement in renal function and structure by specific co-stimulation blockade</li></ul>
<b>Patient Outcomes</b>	<ul style="list-style-type: none"><li>◆ Potential for improved graft and overall survival</li><li>◆ Favorable cardiovascular and metabolic effect</li><li>◆ REMS for novel biologic to better manage risk</li></ul>
<b>Economic Value</b>	<ul style="list-style-type: none"><li>◆ Decreased need for return to dialysis and re-transplantations</li><li>◆ Expanded pool of transplantable organs</li></ul>

# Belatacept: Program and Data Flow

## Submissions

- ◆ US BLA submitted and accepted by FDA; May 1 PDUFA date
- ◆ EU MAA accepted in 1Q 2010

## Data Flow: American Transplant Congress, May 2010

- ◆ Two-year data from core Phase III trials
- ◆ One-year steroid avoidance Phase II data
- ◆ One-year switch from CNI standard of care Phase II data

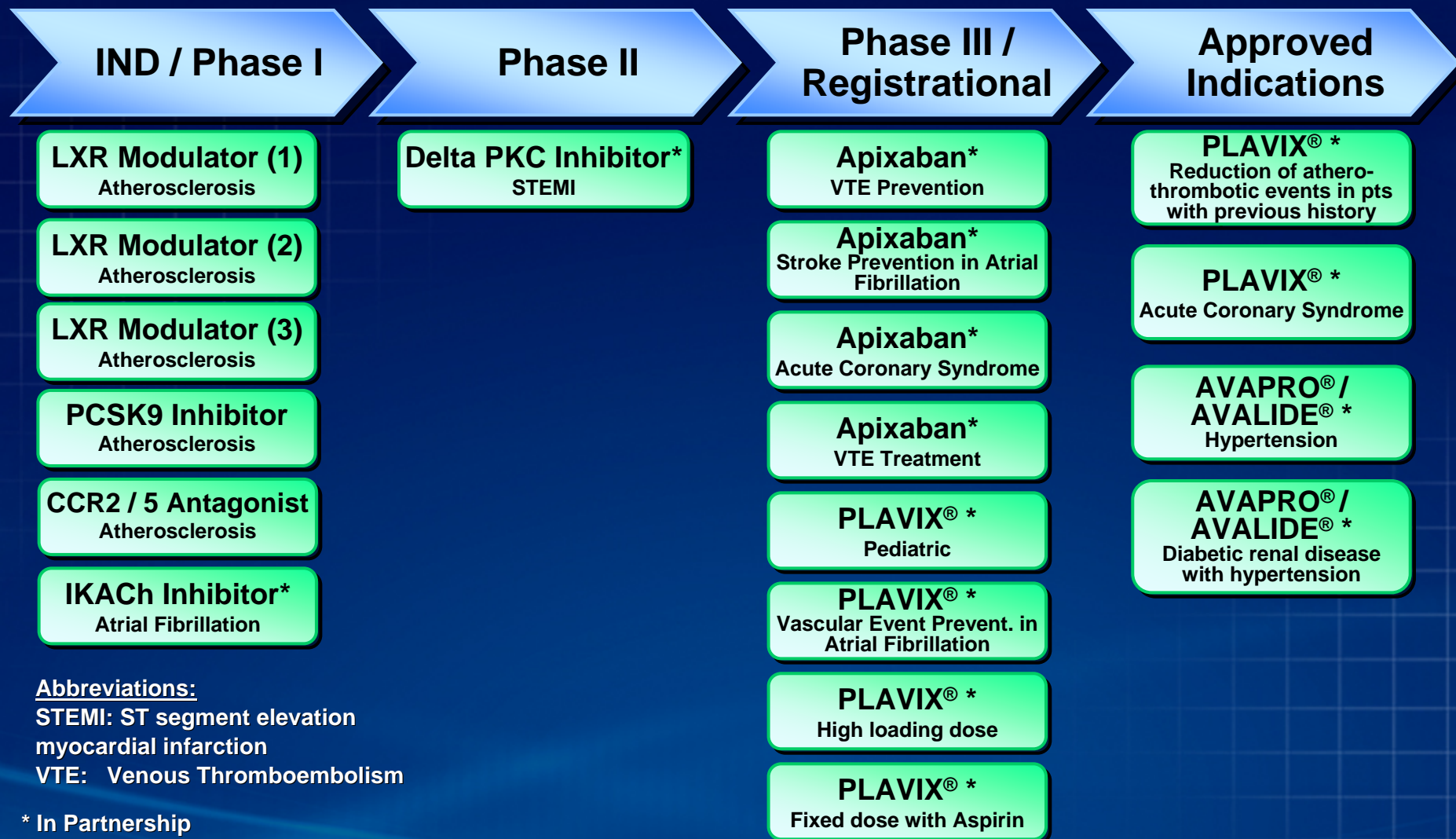
## Ongoing Development

- ◆ Subcutaneous formulation
- ◆ Liver transplant

# Cardiovascular

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# Cardiovascular – Development Portfolio



## Abbreviations:

STEMI: ST segment elevation myocardial infarction

VTE: Venous Thromboembolism

\* In Partnership

Delta PKC Inhibitor: KAI Pharmaceuticals; IKACH Inhibitor: Nissan Chemical and Teijin Pharma; Apixaban: Pfizer; Avapro/Avalide & Plavix: Sanofi-Aventis

# Management of Atrial Fibrillation Remains an Area of Great Unmet Need

- ◆ **Atrial fibrillation is the most common arrhythmia, affecting ~9 million people worldwide**
- ◆ **Atrial fibrillation accounts for ~20% of strokes**
- ◆ **Standard of care (warfarin) has significant limitations: 50% of patients not treated or undertreated**

# Apixaban: A Consistent Anticoagulant with Optimal Benefit / Risk Profile

Mechanism of Action	Efficacy	Safety	Dosing
<ul style="list-style-type: none"> <li>◆ Selective factor Xa coagulation inhibitor</li> <li>◆ Rapid onset of action upstream in coagulation cascade</li> </ul>	<ul style="list-style-type: none"> <li>◆ Consistent anticoagulation</li> <li>◆ Low peak to trough ratio</li> </ul>	<ul style="list-style-type: none"> <li>◆ Low risk of drug interaction</li> <li>◆ Multiple routes of drug elimination</li> </ul>	<ul style="list-style-type: none"> <li>◆ Oral</li> <li>◆ BID dosing</li> <li>◆ No routine monitoring</li> <li>◆ No food effect</li> </ul>
<ul style="list-style-type: none"> <li>◆ Wider therapeutic index than standard of care</li> <li>◆ Optimal benefit / risk profile vs. current standard of care for a large variety of patients</li> </ul>			

# Apixaban: Broad Phase III Development Program (1 of 2)

## Prevention of Venous Thromboembolism (VTE)

Study	N =	Key Features
ADVANCE-1	3,200	◆ Knee replacement surgery vs. US regimen of enoxaparin
ADVANCE-2	3,100	◆ Knee replacement surgery vs. EU regimen of enoxaparin
ADVANCE-3	5,400	◆ Hip replacement surgery vs. global standard regimen of enoxaparin
ADOPT	6,500	◆ Non-surgical medical use vs. enoxaparin

# Apixaban: Broad Phase III Development Program (2 of 2)

## Prevention of Stroke in Patients with Atrial Fibrillation (AF)

Study	N =	Key Features
ARISTOTLE	18,000	<ul style="list-style-type: none"> <li>◆ Head-to-head against warfarin (ARISTOTLE) and aspirin (AVERROES)</li> <li>◆ Unique program that addresses a broad range of AF patients including those who cannot take warfarin</li> </ul>
AVERROES	5,600	

## Acute Coronary Syndrome

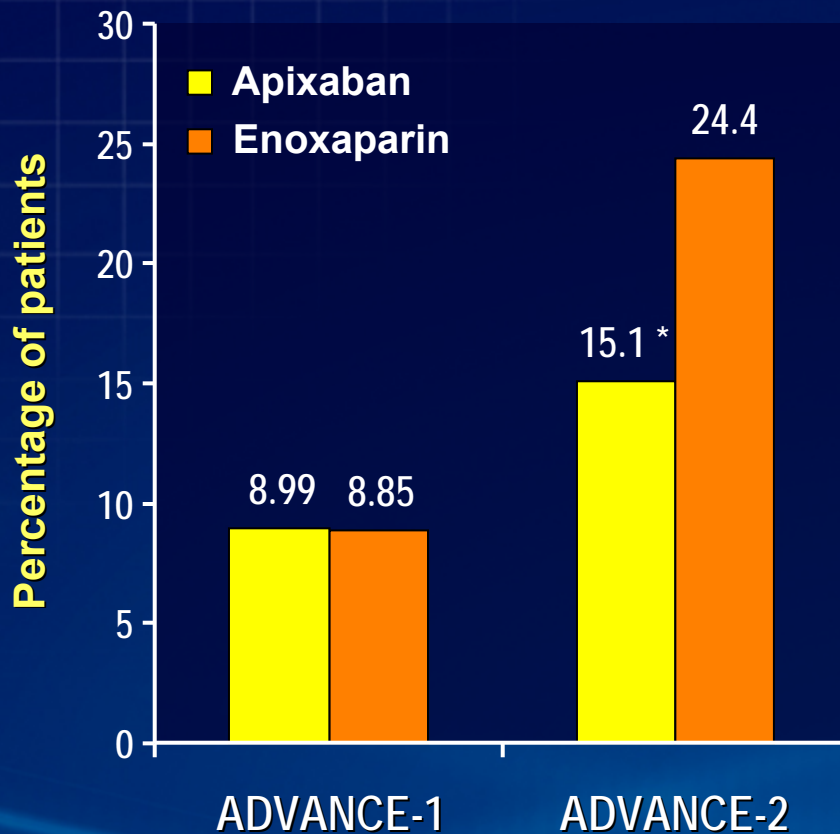
Study	N =	Key Features
APPRAISE-2	10,800	<ul style="list-style-type: none"> <li>◆ Investigate the addition of anticoagulant apixaban to platelet inhibitors in preventing major coronary events</li> </ul>

## Treatment of VTE

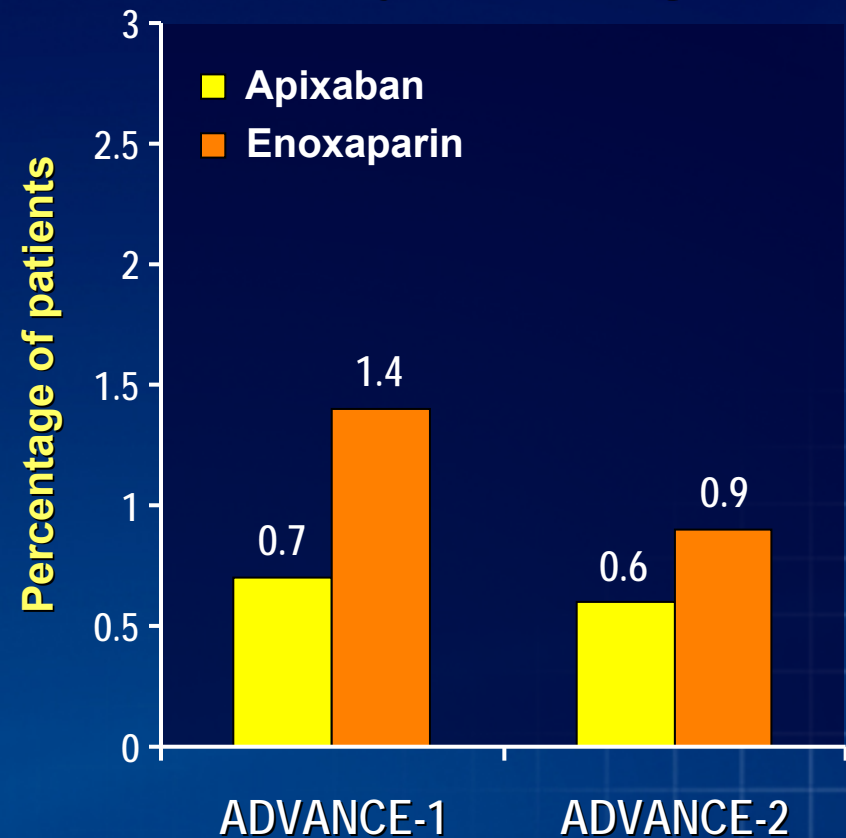
Study	N =	Key Features
AMPLIFY	4,800	<ul style="list-style-type: none"> <li>◆ Six-month study head-to-head against warfarin</li> </ul>
AMPLIFY-EXT	2,400	<ul style="list-style-type: none"> <li>◆ Extended prophylaxis in treated VTE patients of apixaban vs. placebo</li> </ul>

# Apixaban: Phase III Studies in the Prevention of VTE Represent a Balance Between Efficacy and Safety

## Efficacy: All VTE + All Cause Death



## Safety: Major Bleeding



\* statistically significant

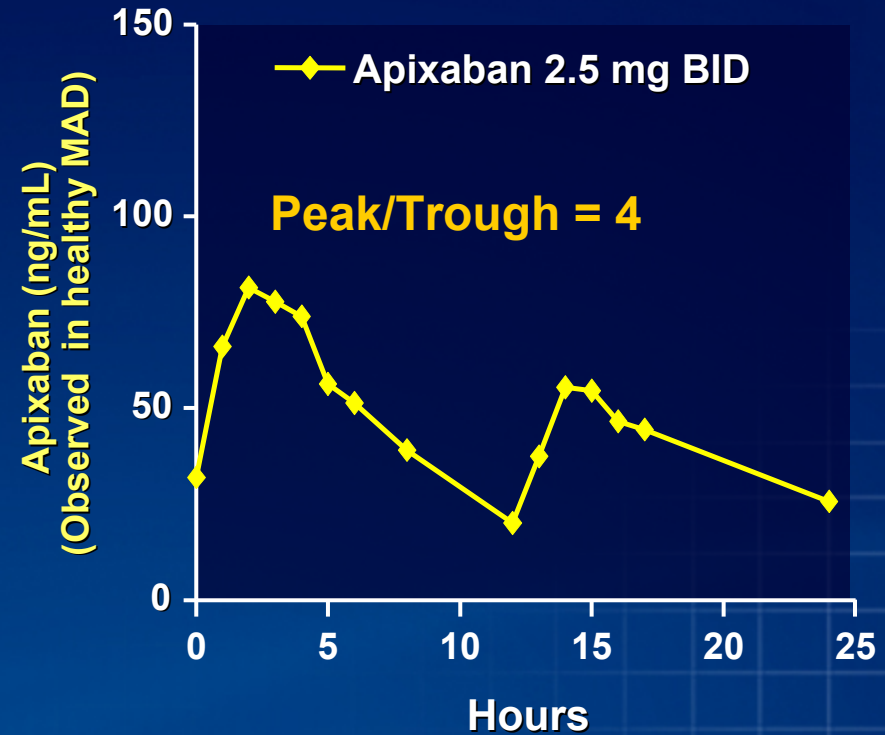
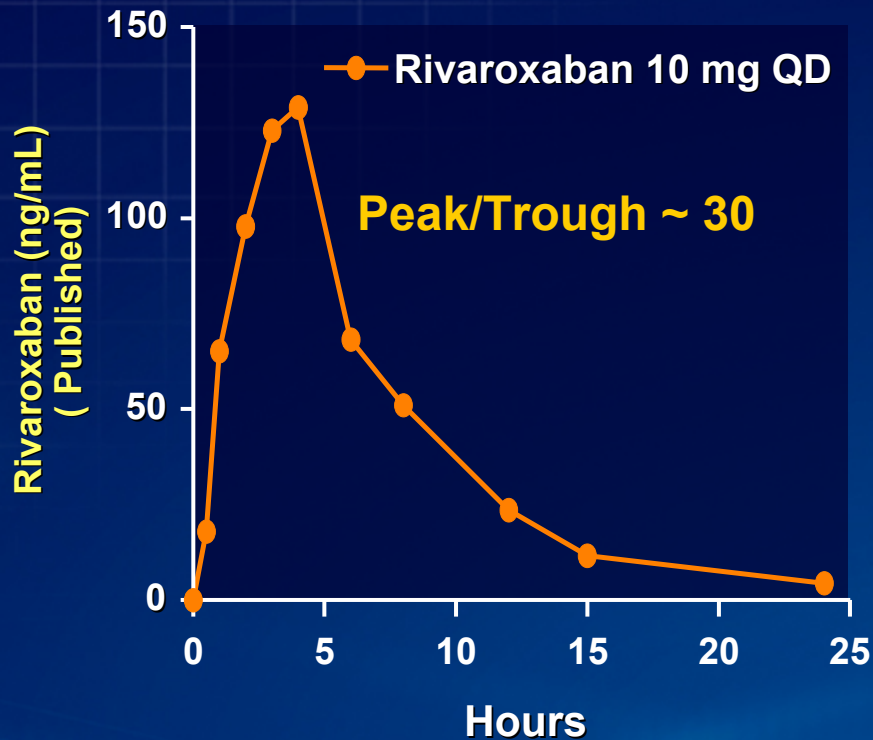
ADVANCE-1: M. Lassen, et al. ASH, December 2008

ADVANCE-2: M. Lassen, et al. ISTH, July 2009

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# Apixaban: Consistent Concentration with BID Dosing is Expected to Reduce Bleeding Complications and Optimize Efficacy

## Plasma Concentration vs. Time Profiles



Apixaban data: Can J Clin Pharmacol 2008; 15(3):e719 (abstr 637).

Rivaroxaban data: estimated from published data in healthy subjects: J Clin Pharmacol 2007; 47: 218-226 Fig 1A.

# Apixaban: Value in Atrial Fibrillation

<b>Challenges</b>	<ul style="list-style-type: none"><li>◆ Warfarin is well established as standard of care despite significant limitations</li><li>◆ Highly competitive area</li></ul>
<b>Differentiation</b>	<ul style="list-style-type: none"><li>◆ A selective factor Xa inhibitor with a wider therapeutic window and optimal benefit / risk profile in a variety of patient types</li><li>◆ Clinical program to demonstrate benefit / risk vs. aspirin in those who cannot take warfarin (AVERROES)</li></ul>
<b>Patient Outcomes</b>	<ul style="list-style-type: none"><li>◆ Potential reduction in stroke as more patients are effectively managed with a consistent anticoagulant</li><li>◆ Well-tolerated, no monitoring required and few drug interactions enabling successful long-term use</li></ul>
<b>Economic Value</b>	<ul style="list-style-type: none"><li>◆ Significant cost associated with warfarin use</li><li>◆ Limitations of use with warfarin leading to treatment gaps</li><li>◆ Strokes are one of the most feared and costly medical outcomes</li></ul>

# Apixaban: Program and Data Flow

## VTE Prevention

- ◆ ADVANCE-3 data has been submitted for presentation at International Congress on Thrombosis (ICT), July 2010
- ◆ Submit in EU 1Q 2010; potential US submission
- ◆ ADOPT data available early 2011

## Stroke Prevention in Atrial Fibrillation

- ◆ Phase II study at Japanese Circulation Society meeting, March 2010
- ◆ Endpoint driven trials: data expected early 2011
- ◆ Potential US & EU submission 2H 2011

## Acute Coronary Syndrome

- ◆ Phase III initiated in March 2009; results expected 2012

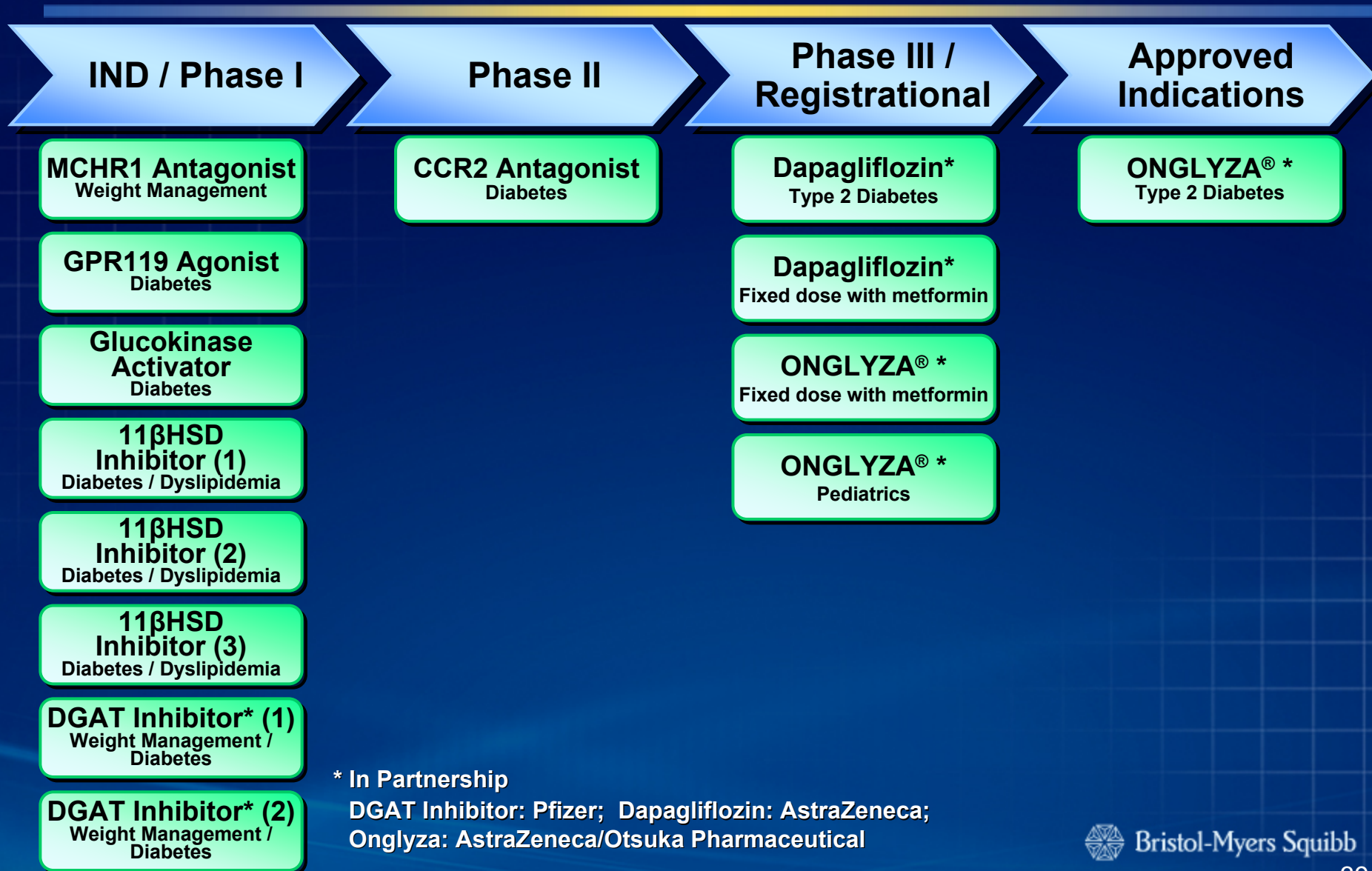
# Metabolics

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# Diabetes: A Growing, Global Epidemic

- ◆ **HbA1c not controlled in 50-70% of patients and fewer reach both HbA1c and blood pressure targets**
- ◆ **Diabetes complications include stroke, heart attack, kidney failure, blindness, leg amputation**
- ◆ **Type 2 Diabetes prevalence expected to grow from 190 million to 360 million by 2030**
- ◆ **India and China will make up nearly 50% of the total number of patients with diabetes in 2030**

# Metabolics – Development Portfolio



\* In Partnership

DGAT Inhibitor: Pfizer; Dapagliflozin: AstraZeneca;  
Onglyza: AstraZeneca/Otsuka Pharmaceutical

# SGLT2 Inhibition Lowers Blood Glucose Levels by Acting on the Kidney Where Glucose is Reabsorbed

## Site of Action of Current Therapies



Pancreas

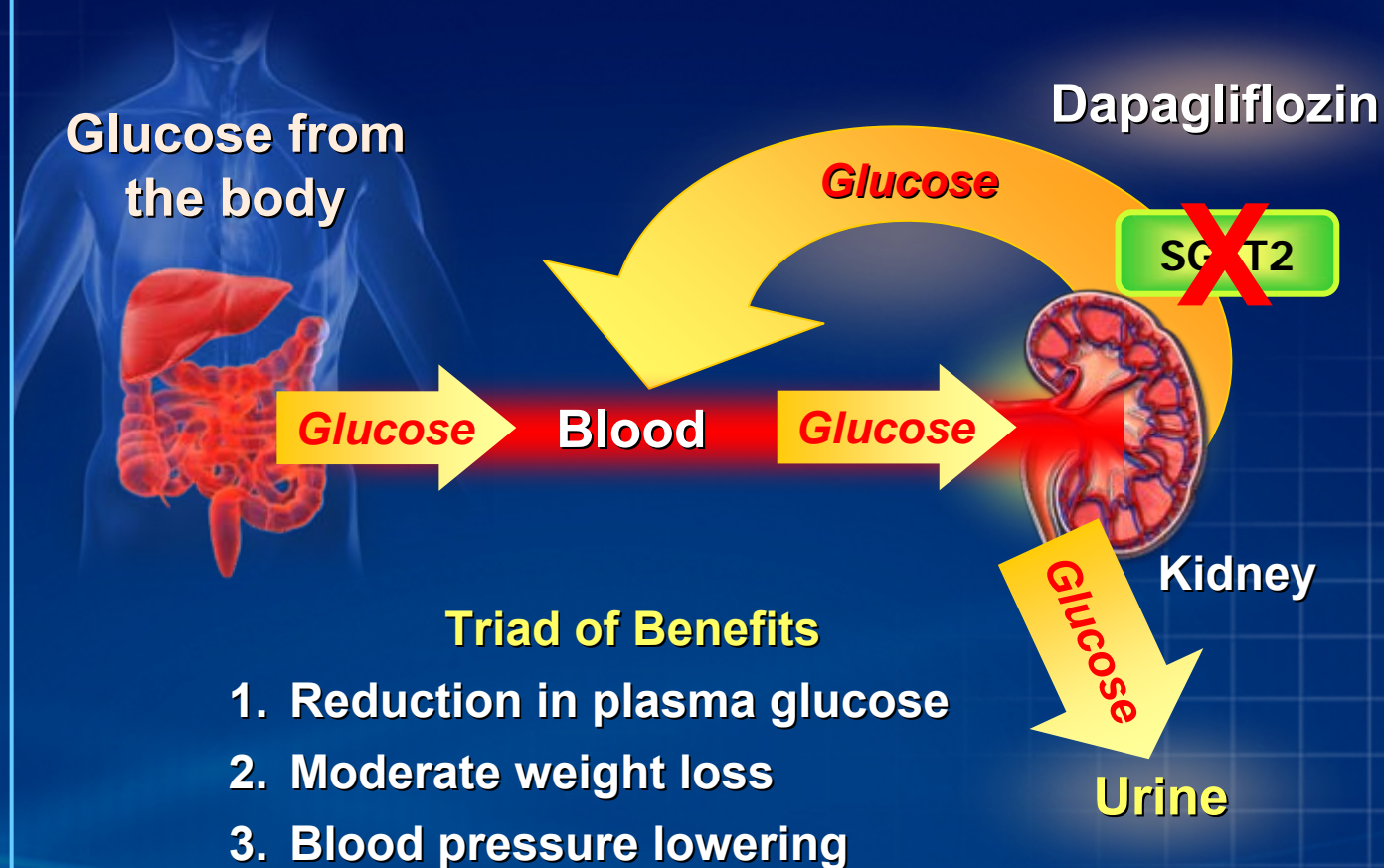


Liver



Muscle

## Dapagliflozin Targets the Kidney



# Dapagliflozin: A Novel Mechanism to Improve the Management of Complex Diabetes Patients

Mechanism of Action	Efficacy	Safety	Dosing
<ul style="list-style-type: none"> <li>◆ Potential first-in-class SGLT2 inhibitor</li> <li>◆ Lowers blood glucose levels by acting on the kidney where glucose is reabsorbed</li> <li>◆ Insulin-independent mechanism delivers efficacy in insulin-resistant patients</li> </ul>	<ul style="list-style-type: none"> <li>◆ Effective at lowering blood glucose</li> <li>◆ Moderate weight loss</li> <li>◆ Blood pressure lowering effect</li> <li>◆ Quick onset of activity</li> <li>◆ Decreased need for insulin in insulin-dependent type II patients</li> </ul>	<ul style="list-style-type: none"> <li>◆ Infrequent hypoglycemia</li> <li>◆ Increase in external genital infections; few with clinical consequences</li> <li>◆ Continue to monitor frequency of urinary tract infections</li> </ul>	<ul style="list-style-type: none"> <li>◆ Oral, once a day</li> <li>◆ Fixed-dose combinations in development</li> </ul>

# Dapagliflozin: Development Program Summary

Patient Population	Therapy type	Study	
Treatment Naïve	Monotherapy	-013, Monotherapy vs. placebo	✓
		-032, Low dose monotherapy	
	Initial combination with metformin	-021 (5mg)	
-034 (10mg)			
Moderately Treatment Experienced	Combination with oral anti-diabetic	-014, Add-on to metformin	✓
		-04, Add-on to metformin vs. sulfonylurea	✓
		-05, Add-on to sulfonylurea	✓
		-030, Add-on to TZD	
Highly Treatment Experienced	Combination with insulin	-06, Add on to insulin	✓
	Combination with other anti-diabetic agents	-009, Reduction in insulin use in insulin-resistant patients (Ph II)	✓
		-029, Renal experience study	



Data presented in 2009



Data targeted for presentation in 2010

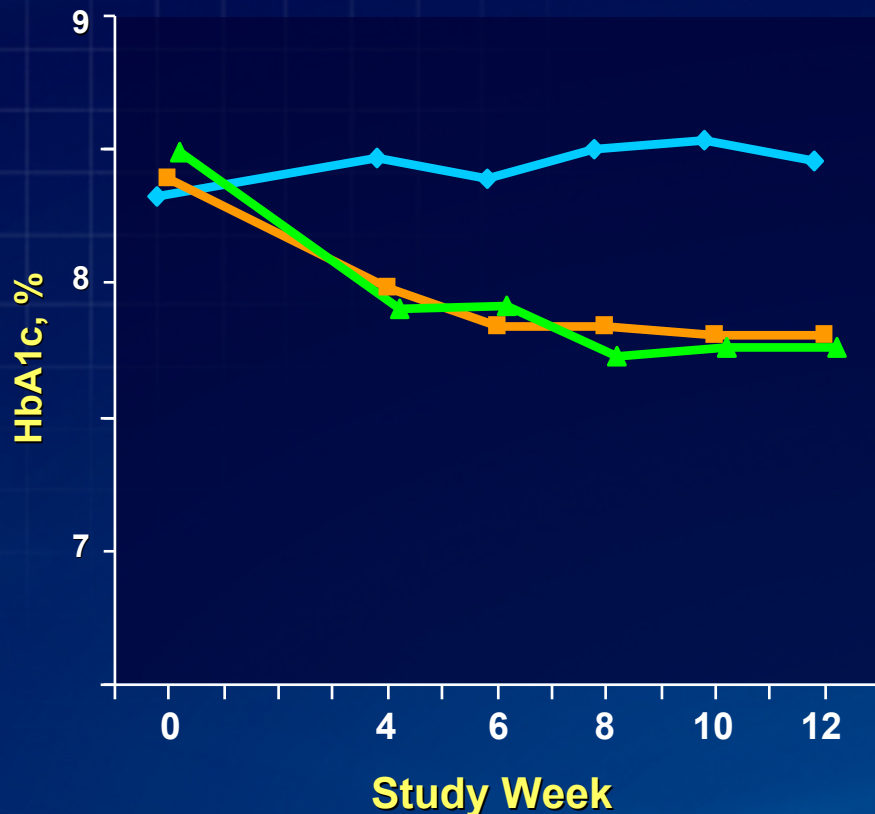
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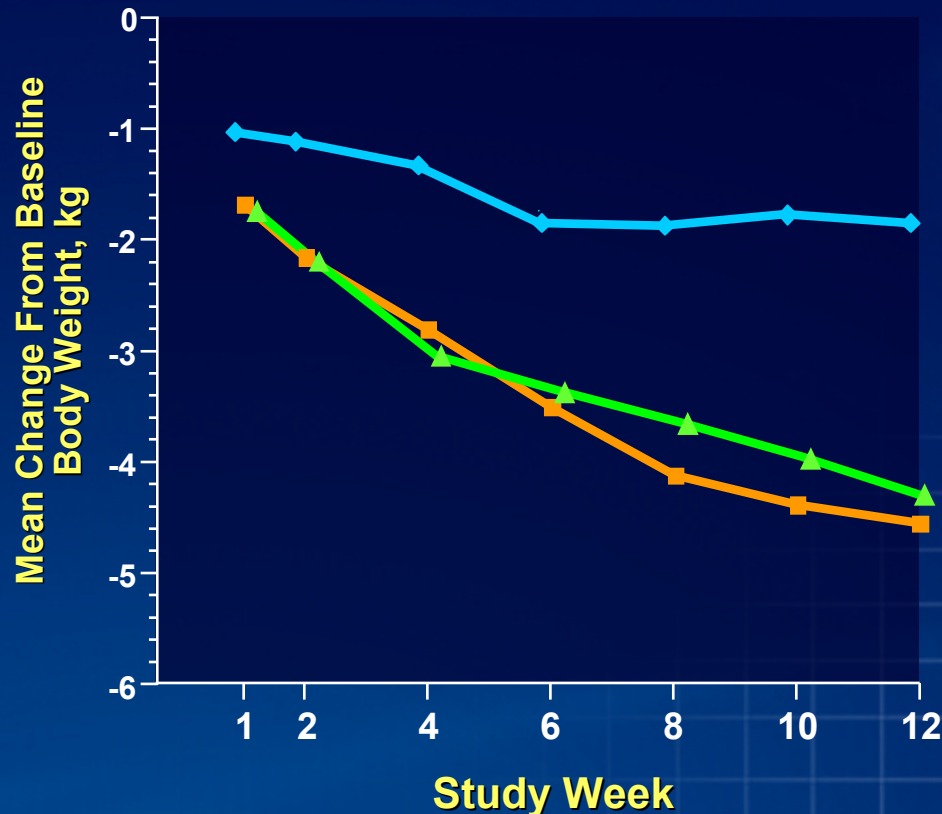
Bristol-Myers Squibb

# Dapagliflozin: Phase II Data Show Improved Glycemic Control & Weight Loss in Patients Uncontrolled on High-Dose Insulin

## HbA1c % change from baseline



## Weight (kg) change from baseline



◆ Placebo + Insulin (n=23)    ■ Dapa 10 mg + Insulin (n=24)    ▲ Dapa 20 mg + Insulin (n=24)

# Dapagliflozin Lowers Blood Glucose and Has Other Beneficial Effects in Type 2 Diabetes

	Add-on to Metformin (-014)				Monotherapy (-013)			
	PBO (N=137)	Dapagliflozin			PBO (N=75)	Dapagliflozin		
		2.5 mg + MET (N=137)	5 mg + MET (N=137)	10 mg +MET (N=135)		2.5 mg (N=65)	5 mg (N=64)	10 mg (N=70)
<b>Standard Diabetes Measures (at Week 24)</b>								
HbA1c Change	-0.30	-0.67*	-0.70*	-0.84*	-0.23	-0.58	-0.77*	-0.89*
FPG Change	-6.0	-17.8*	-21.5*	-23.5*	-4.1	-15.2	-24.1*	-28.8*
<b>Other Beneficial Effects (at Week 24)</b>								
Body Weight Change (kg)	-0.9	-2.2*	-3.0*	-2.9*	-2.2	-3.3	-2.8	-3.2
Systolic Blood Pressure Change (mm Hg)	-0.3	-3.1	-3.5	-5.9	-0.9	-4.6	-2.3	-3.6

\* Statistically significant

Phase III study -014, C. Bailey, et al. EASD, Sept 2009

Phase III study -013, E. Ferrannini, et al. IDF, October 2009

NOT FOR PRODUCT PROMOTIONAL USE

# Dapagliflozin: Additional Clinical Profile

- ◆ **Few cardiovascular events**
- ◆ **Low incidence of hypoglycemia**
- ◆ **Continue to monitor frequency of urinary tract infections**
- ◆ **Increase in genital infections**
  - **Responded to standard treatment**
  - **Rare cause of discontinuations**

# Dapagliflozin: Value in Diabetes

<b>Challenges</b>	<ul style="list-style-type: none"><li>◆ Awareness of the role of the kidney in diabetes</li><li>◆ Characterize and educate on genital and urinary tract safety profile</li></ul>
<b>Differentiation</b>	<ul style="list-style-type: none"><li>◆ Insulin-independent activity improves the control of difficult to manage diabetic patients</li></ul>
<b>Patient Outcomes</b>	<ul style="list-style-type: none"><li>◆ Potential improvement in control in the triad of glucose, weight and blood pressure</li></ul>
<b>Economic Value</b>	<ul style="list-style-type: none"><li>◆ Predictive epidemiologic models underscore the benefits of HbA1c and blood pressure control on patient outcomes</li></ul>

# Dapagliflozin: Program and Data Flow

- ◆ **Additional Ph III data available in 2010 and 2011**
  - **ADA, June 2010**
  - **EASD, September 2010**
- ◆ **EU submission on track for 4Q 2010**
- ◆ **US submission dependent on number of CV events and discussions with FDA**
- ◆ **Ongoing development for fixed-dose combination with metformin**

# Potential for Five More New Medicines to Market by End of 2012

**onglyza**  
(saxagliptin)

Bringing a new choice to the management of diabetes

**Ipilimumab**

Establishing a new immunotherapy paradigm for the treatment of cancer

**Brivanib**

Novel dual kinase inhibitor with broad anti-cancer potential

**Belatacept**

Novel co-stimulation blocker developed as an alternative cornerstone therapy in solid organ transplantation

**Apixaban**

Oral Factor Xa inhibitor with potentially optimal risk/benefit balance providing consistent anticoagulation

**Dapagliflozin**

Providing a new insulin-independent mechanism for potentially improved outcomes in overweight and obese diabetes patients